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THE
AMERICAN
SURGEON

Vol. 22, No. 9 September, 1956

PREVENTION AND MANAGEMENT OF COMPLICATIONS OF ILEOSTOMY AND COLOSTOMY

AMBROSE H. STORCK, M.D.*

New Orleans, La.

There are no other commonly performed surgical procedures which are followed by more frequent and varied complications than those which are associated with ileostomy and colostomy. In addition to the complications which may follow any surgical procedure of considerable magnitude, there are certain complications that are either peculiar to, or at least more likely to occur in patients upon whom an ileostomy or a colostomy is performed, and it is to the prevention and management of these complications that particular attention will be directed. The nature, frequency, and preventability of at least some of these complications bears a relationship to the age of the patient, the developmental, traumatic, inflammatory or neoplastic lesion for which ileostomy or colostomy is performed and to other operative procedures which are sometimes performed at the same time.

Since a constantly increasing number of persons are requiring the performance of an ileostomy or a colostomy, and since they will be living for a progressively longer time after these operations, it becomes more and more necessary to consider ways and means whereby they will not only survive the operative procedures, but to insure that they will be as free as possible of physical and emotional complications.

ILEOSTOMY DYSFUNCTION

The most serious common complication associated with ileostomy is so-called ileostomy dysfunction, a condition about which there has been great misunderstanding. Evidences of ileostomy dysfunction include cramp-like pains, watery discharge from the stoma (1000 cc. or more daily), vomiting at times and a shock-like state due to water and electrolyte deficiencies. All too frequently this de-

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Presented during the Richmond Assembly of The Southeastern Surgical Congress, March 12–15, 1956, Richmond, Virginia.

pleting complication has been considered to be related to food intake, to impaired digestive function or to other factors, whereas the actual cause, i.e., obstruction of the small bowel with resulting distention and consequent hypersecretion, has been overlooked or has not been fully appreciated. This complication may exist in either an acute or a chronic form and may make its appearance at any time following the first postoperative day, usually occurring initially at some time between the first day and the third week following operation and most commonly at the middle or end of the second week. Causes to which early obstruction leading to ileostomy dysfunction may be due, include compression of the ileum in its course through too narrow a passageway in the abdominal wall, postoperative edema of the bowel wall; serositis (localized peritonitis); or compression by granulation tissue. The late or chronic form of ileostomy dysfunction usually is due to constriction of the bowel by scar tissue in the abdominal wall around the stoma, particularly at the level of the skin.

Early prophylactic measures for averting ileostomy dysfunction are directed toward averting or promptly relieving distention of the ileum, in order to prevent ensuing hypersecretion which otherwise results. The most effective way of accomplishing this is by providing intermittent catheter drainage for 4 of every 5 hours, in order to evacuate both gas and fluid. This method of decompression is supplemented by the administration of a low residue diet and by mild digital dilatation of the stoma.

For the prevention or relief of stomal obstruction responsible for the later-appearing and persistent or what might be called chronic forms of ileostomy dysfunction, one or more of a number of procedures of varying effectiveness have been devised and may be employed with more or less success. Excision of a wafer of skin at the site of the stoma with the hope of preventing constriction of the ileum by scar contracture at the skin level has been tried but unfortunately is not consistently or even usually effective. Rather remarkably, however, the excision of scar tissue and a ring of skin to relieve constriction of a matured ileostomy usually is permanently effective. Mucosal or skin grafting of the stoma at the time of primary operation or as a secondary procedure has been extensively tried and generally is considered to be frequently effective in reducing the incidence of stomal constriction. When stomal obstruction is due to granulation or scar tissue above the level of the skin, relief may at times be afforded by making multiple radial incisions through the granulation or scar tissue. Under some circumstances the only way to achieve relief of ileostomy dysfunction due to a malformed or malfunctioning ileostomy is to create an entirely new stoma.

The potentially fatal fluid balance, electrolyte and nutritional disturbances which rapidly develop as an accompaniment of ileostomy dysfunction makes it imperative that these complications be anticipated and constantly kept in mind during the entire period of surgical management, beginning during the preoperative phase and continuing until thorough stabilization of the patient has occurred. During the most critical periods there should be frequent clinical and laboratory surveys and assessments of the patient to determine his fluid, electrolyte, blood transfusion, vitamin, general nutritional and other requirements.

STENOSIS OF STOMA

Stenosis of some extent occurs in many if not most ileostomies and colostomies. In its lesser degrees, stenosis causes no considerable inconvenience, discomfort or other disturbance, and possibly may even serve a desirable purpose in the control of discharge from the stoma. Whereas the lesser stenoses are usually well tolerated and may even be of some benefit, undesirable narrowing of the stoma may greatly annoy and deplete the patient and vex the surgeon.

Causes of stomal stenosis include: (1) compression of the bowel due to a passageway through the abdominal wall which at some point was not made large enough at the time of operation; (2) tension, due to insufficient length of the limb or loop of bowel; (3) acute angulation; (4) edema of the bowel itself or of the abdominal wall passageway, due to trauma or infection; (5) serositis; (6) granulation tissue or scar tissue around stoma; and (7) neoplastic infiltration.

From a consideration of the foregoing list of causes it is evident that several and, incidentally, some of the commonest causes of stomal stenosis are due to errors in judgment or technic on the part of the surgeon, and the manner of preventing stomal stenosis due to such causes is obvious. Some of the other causes of stomal stenosis cannot very well be prevented. A number of the methods which have been employed for the intended prevention or treatment of stomal obstruction due to a variety of causes are reviewed in the preceding section on Ileostomy Dysfunction. In the instance of colonic stomal stenosis just as in the instance of ileal stomal stenosis which cannot be satisfactorily managed by repeated dilatation, minor or major surgical revision of the stoma or even the creation of a new stoma must be undertaken.

NECROSIS OF STOMA

Necrosis of an intestinal stoma is most commonly the result of deficient blood supply caused by: (1) surgical occlusion of the arterial supply to the part; (2) tension of the bowel due to too short a limb or loop of bowel: (3) compression of the bowel by the abdominal wall due to too small a passageway or (4) compression by a too tightly fitting flange of an ileostomy or colostomy bag. The prevention of this complication usually is possible by simply anticipating and avoiding the foregoing causes. To permit early recognition of impending or established necrosis of the stoma, it should be frequently inspected, especially during the first 24 hours following operation and at least once daily for several days afterwards. If it appears that necrosis is impending, prompt action should be taken to relieve tension or compression by removing the tube or rod underlying an exteriorized loop if it appears that either of these procedures can be done without likely retraction of the bowel. If there is reason to believe that compression by the abdominal wall is the responsible cause, the abdominal passageway should be explored and enlarged. If the already mentioned causes are not found or if relief is not afforded by the foregoing methods of attempted relief, then the abdomen should be opened and viable bowel brought out at the same or at a higher level.

RETRACTION OF STOMA

Retraction of the stoma usually can be averted by: (1) providing a sufficiently long and mobile loop or limb of bowel; (2) choosing such a site for the exit of the bowel through the abdominal wall that the bowel will not be under tension; (3) preventing or aggressively treating abdominal distention by means of either a long or a short single or double lumen tube introduced through the nose and into the stomach and intestine—it is often advantageous to institute gastrointestinal suction drainage preoperatively, especially if at that time there is considerable abdominal distention; (4) preventing ischemic necrosis of the stoma and adjacent bowel by observing the precautions which are discussed under the heading Necrosis of Stoma; (5) reapplying a clamp partially across the ostomy immediately after the initial opening of the ostomy; (6) employing plain gauze dressings which adhere to the exteriorized bowel, and delaying the removal of such dressings about the stoma until the fourth postoperative day unless opening of the stoma at the time of operation and immediate application of a flange-type bag is considered desirable and is feasible; (7) inspecting the stoma early and frequently, especially after removal of the clamp placed across it at the time of operation, in order to reveal any beginning retraction.

If definite retraction of the stoma occurs it usually is advisable to create a new stoma at the same level or at a higher level.

PARAOSTOMY FISTULA

The causes of fistulas alongside or near intestinal stomas include: (1) damage to the bowel during operation caused by rough handling; (2) introduction of sutures into the bowel wall for the purpose of fixing it to the abdominal wall; (3) pressure against the bowel by the flange or the rim of the ileostomy or colostomy bag; (4) injury of the bowel by an irrigation catheter; and (5) too vigorous digital dilatation. Ordinary precautions to avoid the foregoing causes constitute the obvious means of preventing this complication, which is more likely to develop about an ileostomy than about a colostomy.

The practice of introducing sutures into the wall of the ileum for the purpose of fixing it to the abdominal wall is probably the most common cause of paraileostomy fistula, and is a procedure which should be avoided because it is not only unnecessary but because it is not without danger. Even in the instance of the colon, it is advisable to avoid introduction of fixation sutures into the bowel wall and to instead accomplish any fixation which may seem advisable by tacking two or more epiploic appendages to the peritoneal suture line.

In fitting the flange of an ileostomy or a colostomy bag, a clearance of 5 millimeters should be provided between the stoma and the opening in the flange or the rim of the bag, as the case may be.

If a paraostomy fistula develops, and does not close spontaneously after a period of several weeks, either minor or major revision of the stoma should be undertaken or a new stoma should be created.

DERMATITIS IN REGION OF OSTOMY

This annoying and sometime quite serious complication can be prevented or managed by several means:

1. Placement of the stoma in an area where the abdominal wall contour, including the absence of bony prominences, makes for favorable fitting of an ileostomy or colostomy bag. 2. Prevention of maceration of the skin adjacent to an intestinal stoma which follows the use of petrolatum gauze, ointments and powders, by using plain dry gauze dressings from the start. 3. Use of one or another of the several presently available flange-bags as soon as the ostomy is opened, whether at the time of operation or later. As the ostomy matures, appropriate changes in the size of the opening in the flange should be made from time to time in order to provide a close but nonconstricting fit of the flange around the stoma. 4. If, as a result of some inadvertence, dermatitis about the stoma occurs, then it may be necessary to apply a skin protective such as aluminum or kaolin paste, silicone or compound tincture of benzoin or to keep the patient face down on a Stryker frame or some similar device until the dermatitis has improved sufficiently to initiate or resume the use of a flange-bag.

PARAOSTOMY HERNIA

The incidence of hernias around or alongside intestinal stomas can be reduced by: (1) providing an exit, whether it be a stab wound or a part of the principal incision, which is not unnecessarily large but which just allows snug clearance; (2) selecting a site on the abdominal wall which is near the mid-transverse extent of the rectus abdominis muscle and which at the same time is above the semilunar fold of Douglas, rather than in the often chosen low iliac regions where there is no posterior rectus sheath; (3) removing epiploic appendages from that portion of the bowel which will traverse the abdominal wall, thus reducing the required size of the exit wound and also eliminating the wedging action exerted by the epiploic appendages; and (4) preventing wound infection.

Small paraostomy hernias usually require no special management since they cause little or no discomfort or other disturbances, and can be adequately retained by a properly fitting ileostomy or colostomy bag or dome. In some instances widening or other modification of the belt which most patients wear to hold the bag in place can be done in such a way as to satisfactorily retain the hernia. Except in the rare instances in which incarceration or strangulation occurs, or in which great size or other unusual circumstances more or less demand it, operative surgical procedures for paraostomy hernias are not necessary nor are they likely to be rewarding.

PROLAPSE OF STOMA

Slight prolapse of the stoma is common, is of no great consequence, and demands no major corrective procedure. On the other hand, extensive prolapse of an intestinal stoma may be a very serious and challenging complication.

Lack of complete understanding concerning the cause and mechanism of some of the major forms of prolapse of either the ileum or the colon adds to the difficulty of relieving this condition. The existence of too large a tract in the abdominal wall probably is only occasionally an important or sole responsible factor.

In its milder forms, prolapse of the stoma can be satisfactorily controlled by the conventional ileostomy or colostomy bag, or by domes or caps especially designed for that purpose. For the correction of extensive prolapse which cannot be satisfactorily managed by simple measures, a variety of surgical procedures have been suggested. These procedures, which have been applied with varying degrees of success include: (1) resection of additional bowel; (2) suture of the prolapsing bowel to adjoining loops of bowel; (3) narrowing of the tract in the abdominal wall internally, or (4) narrowing of the tract in the abdominal wall externally, in a manner similar to the Thiersch operation for relief of rectal prolapse, which consists of the subcutaneous introduction of a partially constricting circular suture of nonabsorbable material, usually wire.

SEVERE POSTOPERATIVE DISTENTION

Unless certain preoperative and postoperative precautions are taken, a serious degree of abdominal distention may occur following the performance of either ileostomy or colostomy. To prevent or minimize this distressing and sometimes quite dangerous complication the following measures may be employed: 1. Preoperative and early postoperative institution of gastrointestinal suction-drainage by means of long or short tubes of either the single or double lumen variety. The Rawson-Abbott tube has the advantage of providing for both gastric and upper small bowel decompression. When employing any type of gastrointestinal suction-drainage caution must be observed to avoid dangerous fluid and electrolyte losses which may result from the uninterrupted or too prolonged withdrawal of gastrointestinal secretions. Preoperative decompression of the gastrointestinal tract by means of tube drainage provides the additional advantage of permitting, with minimum trauma, any inspection or palpatory exploration which may be considered advisable in areas remote from the immediate area of the operative procedure. In performing ileostomy, it should be kept in mind that as a rule best results follow an operative procedure which is as simple and expeditious as possible, usually with avoidance of any extensives exploratory procedures. 2. Thorough preoperative evacuation of the colon by purgation with castor oil or sodium phosphate. 3. Preliminary cecostomy or transverse colostomy may be necessary if complete or nearly complete low obstruction of the colon makes impossible the proper mechanical antibiotic and chemotherapeutic preparation of the colon for definitive surgery. 4. Avoidance of compression of the bowel in its course through the abdominal wall, by providing a sufficiently large passageway either through a stab wound or through a portion of the principal incision. 5. Immediate or at least early opening of the stoma, which with proper preoperative preparation of the bowel can at the present time be done with safety. 6. Repeated early introduction of a catheter through the stoma, which if not

done in the instance of ileostomies may lead to the development of ileostomy dysfunction. 7. Minor or major revision of a constricting stoma or even the creation of a new stoma which may at times be necessary to relieve persistent severe distention.

URINARY RETENTION AND INFECTION

These very common complications associated with colostomies performed as a part of abdominoperineal resections of the colon must be anticipated as a result of disturbed bladder innervation, displacement of the bladder or prostatism. It usually is not possible to entirely prevent these sequellae although at times a preliminary transurethral resection of obstructing prostatic tissue may be helpful when prostatic hypertrophy exists. An indwelling Foley catheter should be introduced preoperatively or immediately postoperatively and should be allowed to remain in place for 7 to 12 days when colostomy is performed in conjunction with abdominoperineal resection of the rectum. During this period a urinary antiseptic should be administered either orally or parenterally.

DIFFICULTY IN CARING FOR THE STOMA

Factors which may be responsible for the patient having difficulty in caring for the stoma include: (1) an abdominal contour or the existence of multiple or extensive scars which makes it impossible to provide ideal placement of the stoma; (2) improper choice of site for the stoma; (3) inadequate instruction of the patient; (4) ineptness of the patient; or (5) poorly fitting or inappropriate ileostomy or colostomy equipment.

The prevention and management of difficulty in caring for the stoma usually can be averted or satisfactorily managed by preoperative study of the contour of the abdomen by the surgeon, and by proper placement of the stoma; additional instructions and reassurance of the patient, and by acquisition of correct equipment by the patient. Occasionally the creation of a new stoma may be necessary.

DIARRHEA FOLLOWING COLOSTOMY

Periodic diarrhea following colostomy is quite common and usually is related to the consumption of certain foods including green corn, baked beans, greasy and fried foods. Patients who have had a colostomy should be advised to avoid such foods or to eat them only occasionally and sparingly.

For the relief of diarrhea in a patient with a colostomy the commonly used methods for relief of this condition under ordinary circumstances are equally applicable, and include the drinking of scalded skimmed milk, and the administration of bismuth bicarbonate, kaolin-pectin mixtures or other similar preparations.

EMOTIONAL DISTURBANCES

The natural aversion to either an ileostomy or a colostomy requires careful thought and judicious action on the part of everyone who plays a role in the

many phases of management of a patient who is to have or who has had such an operation. Assistance to the patient in meeting the psychologic problems is needed from the very first time the matter of having to have an ileostomy or a colostomy is faced by the patient. The first physician who broaches the matter the surgeon, the nurses, the relatives and friends, as well as the fitter of the devices which the patient will have to wear must all in their various capacities give proper assistance to the patient. Another person who has an ileostomy or a colostomy often can be of incalculable help in reassuring the patient by example. In most instances it is advisable to avoid much preoperative discussion of the matter. Careful instruction and demonstration which will develop self-reliance and the ability for self-care should be provided before the patient leaves the hospital. When the patient returns home the visiting nurse can play an important role but her services should not be continued too long. Detailed printed instructions concerning care of the ileostomy or colostomy and the diet are helpful. The presently available better fitting, less conspicuous and disposable ileostomy and colostomy equipment including improved irrigating devices and retaining or protective domes which facilitate and expedite self-care and add to self-confidence, have done much to relieve emotional tensions of the ileostomy or colostomy patient. A matter of extreme importance to the patient is the maintenance of sustained interest by the surgeon as well as other persons to whom he looks for reasonable but not undue understanding and help.

MISCELLANEOUS AND RARER COMPLICATIONS

In addition to the complications which have been discussed, others which are either less specifically related to ileostomy and colostomy or which, although related are less common, include: (1) intestinal obstruction; (2) bleeding from the ileum or the colon; (3) perforation of the ileum or colon, occurring either spontaneously or as a result of the introduction of an irrigating catheter; (4) perineal evisceration following abdominoperineal resection of the rectum; (5) peritonitis due to transmural contamination.

Early recognition and the prompt institution of appropriate conservative or operative treatment of the complications can result in the survival of many of the patients who develop the serious complications listed in the preceding paragraph.

MORTALITY FOLLOWING ILEOSTOMY AND COLOSTOMY

Outstanding among the precautionary and preventive measures and policies which have greatly reduced the incidence of death following the creation of intestinal stomas and particularly ileostomies performed on severely ill patients, are the following: 1. Adequate preparation of the patient from the standpoint of fluid, electrolyte, blood volume and nutritional requirements, in order to permit survival despite the stresses and metabolic disturbance produced by anesthesia, operative surgical manipulations, postoperative intestinal distention and possibly infection. Emergency operations on acutely ill and poorly prepared patients should rarely if ever be undertaken. 2. The appropriate admin-

istration of blood transfusion, adrenal cortex preparations, vitamins and antibiotics have all been adjuncts in lowering mortality. 3. A better understanding of the relationship of ileostomy dysfunction to distention of the small bowel and consequent greater attention to the matter of preventing or overcoming stomal obstruction at all times following operation.

SUMMARY

The complications which occur following ileostomy and colostomy include those due to poor surgical judgment or technic, improper preoperative preparation and inadequate postoperative care, insufficient instruction of the patient and failure to see that he is provided with proper equipment, and certain unpreventable complications which are due to the extremely poor condition of some patients upon whom such operations must be performed. The causes, methods of anticipating and preventing as well as managing the complications of ileostomy and colostomy are reviewed.

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BACTERIAL FACTORS IN STRANGULATION OBSTRUCTION: REVIEW OF EXPERIMENTAL WORK

ISIDORE COHN, JR., M.D.

New Orleans, La.

The role of bacteria in strangulation intestinal obstruction has been debated almost since the first serious work in this field[12] was begun. Many ingenious approaches to the problem have been devised in an attempt to better evaluate the bacterial factor alone. Unfortunately, most of these approaches have had some defect. It remained for the advent of the antibacterial agents to make possible the study of strangulation obstruction with adequate control of the bacterial factors. Numerous advances since the introduction of antibacterial agents justify a review and correlation of the new aspects of the problem.

Prior to the introduction of the antibacterial agents, life of an animal with strangulation intestinal obstruction had been prolonged when the segment was not so long as to cause death from shock due to blood loss, blood and fluid replacement were adequate, electrolyte balance was well maintained, and postoperative care was as careful as that given to patients. However, even all these aids did not prevent death in strangulation obstruction.

Re-evaluation of the problem with a standard type of strangulation obstruction in dogs and with careful postoperative care seemed desirable.[34] Obstruction was produced by dividing the bowel and closing its two ends. Strangulation was produced by dividing all veins to a 30 cm. segment of the obstructed bowel. In the postoperative period large amounts of blood and electrolytes were used, the animals were carefully observed, and studies were repeated at frequent intervals. Average survival was increased to 36 hours in contrast to survivals of 7 to 24 hours achieved by previous workers. The animals remained in good condition until just a few hours before death when a sudden change occurred in their clinical condition in association with changes in the peritoneal fluid. Cultures from the early peritoneal fluid usually were negative. Cultures from the late peritoneal fluid revealed the organisms previously present in the lumen of the bowel, even in the absence of frank perforation. Neither bacteremia, shock, nor electrolyte imbalance were thought to play a role in the death of any of the animals. The late peritoneal fluid contained a pigment which produced an unusual spectrophotometric curve not similar to anything previously reported. This pigment was first detected in the lumen of the strangulated segment and was found in the blood stream after it appeared in the peritoneal fluid. When the peritoneal fluid changed its characteristics, there were significant elevations in the nitrogen components of the peritoneal fluid, followed by similar

From the Department of Surgery, Louisiana State University School of Medicine, New Orleans, Louisiana.

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changes in the nitrogen composition of the blood. These studies demonstrated that adequate blood, plasma, and electrolyte support would not indefinitely prolong life in dogs with strangulation obstruction, and suggested the presence of some toxic agent.

The toxic theory was tested by studying the lethal properties of the peritoneal fluid.[35] The early, unchanged peritoneal fluid was without effect when injected intraperitoneally or intravenously into normal dogs. The late peritoneal fluid was lethal in much smaller quantities. Thus some undefined lethal agent was presumed to be present in the late peritoneal fluid.

Clinical confirmation of the bacteriologic and spectrophotometric abnormalities would be of great value. Seven large Philadelphia hospitals were observed for two years.[5, 13] Peritoneal fluid from 18 patients was available for study and the records of these patients were carefully analyzed. Each portion of the study was done independently to remove bias as much as possible. Spectrophotometric abnormalities similar to those found experimentally were observed in only a single case.[18] Positive bacteriologic findings were more common. The clinical findings could be correlated better with the bacteriologic results in the peritoneal fluid than with the spectrophotometric findings.

Further attempts to identify the toxic agent in the peritoneal fluid have included attempts at *in vitro* reproduction of the spectrophotometrically abnormal pigment.[36] The various contents of the strangulated loop were incubated under conditions that would permit extensive bacterial growth. A similar, but not identical, abnormal pigment was produced by mixing blood and activated pancreatic juice, and this mixture was lethal when given intravenously. However, activated pancreatic juice and plasma also were lethal without producing the abnormal pigment. All such mixtures contained one or more of the bacteria usually found in the strangulation obstruction experiments. It was not possible to produce the abnormal spectrophotometric curve using Seitz-filtered pancreatic juice, although the addition of bacteria to such a sterile mixture would yield the abnormal pigment. Thus bacteria were not even eliminated in experiments designed to study the toxicity of pancreatic secretions. Further studies utilizing known concentrations of bacteria failed to show a distinct correlation between the bacterial content of these fluids and their toxicity, but bacterial exotoxins were not excluded by these studies.[37]

While the experiments just detailed did not eliminate bacteria in their attempt to implicate pancreatic secretions as the toxic agent in strangulation obstruction, other experiments demonstrated that strangulation obstruction could be lethal in the absence of pancreatic secretions.[16] The use of a modified Mann-Williamson operation which served to divert all duodenal contents to the lower small bowel, followed at a later date by the creation of a strangulation obstruction above the re-entrance of biliary, pancreatic, and duodenal secretions showed that death was not prevented under these circumstances. This eliminated pancreatic secretions as an essential element in the toxicity of strangulation obstruction.

It has been noted previously that the later peritoneal fluid in strangulation

obstruction often had a bacterial spectrum similar to, or identical with, that of the bowel lumen. The organisms most frequently found were *Cl. welchii*, *E. coli*, and streptococci. Of these three, the toxins of *Cl. welchii* are the most profuse, the most lethal, and the ones most likely to produce several changes noted experimentally—hemolysis, noncoagulability, and absence of a purulent reaction in the peritoneal fluid; and certain histologic changes in various organs. Other evidence has recently pointed to the importance of *Cl. welchii*. Lecithinase, the major toxin of *Cl. welchii*, was found in the appendiceal fluids of 89 per cent of dogs with experimental appendicitis.[43] This toxin was held responsible for many alterations in hemodynamics and hepatic function and a severe toxemia followed its absorption. The same toxin, found in the obstructed, strangulated small intestine of 91 per cent of dogs studied, was considered one of the significant factors in the death of dogs with strangulation intestinal obstruction.[1] The inability to detect lecithinase in the blood was attributed to its binding by the red blood cells, since it was easily found in the thoracic duct after strangulation obstruction.[24, 30, 31] Hyaluronidase, another welch toxin not found in the normal bowel, was found in significant quantities in the bowel of dogs with strangulation obstruction, and thought to increase bowel-wall permeability.[44] The peritoneal fluid increased capillary permeability[28] and this may have played a role in producing some of the shock seen in strangulation obstruction.

Isolated, free segments of bowel in the peritoneal cavity of normal dogs were lethal, although sterile bowel was without effect.[17, 29] This indicated that the death in strangulation obstruction was not due to the absorption of noxious agents arising from autolysis of the bowel wall alone. Sterile loops of bowel, injected with sublethal doses of pure cultures of *Cl. welchii*, produced a fatal result,[17] further indicating the important role of these organisms in strangulation obstruction.

The earliest studies utilizing antibiotics demonstrated that penicillin significantly improved the survival of animals with a closed loop.[25] This work demonstrated that marked distention of a loop in the presence of bacteriostatic agents was compatible with life, that uninhibited bacterial growth was compatible with life in the absence of distention, and that distention must precede infection of the intestinal wall by the normal intestinal flora. Massive doses of penicillin also helped to preserve viability in segments of bowel with only temporary occlusion of the venous blood supply.[27] Thus the first work with antibiotics demonstrated the importance of bacteria or their products as a cause of death in obstruction.

Postoperative penicillin prolonged survival for a significant but limited period in strangulation obstruction of the small bowel.[2, 3, 4] Penicillin was thought to prevent toxemia by delaying or completely inhibiting invasion of the bowel wall. Since death did occur, and since there were gross and microscopic evidences of damage in the strangulated segment, it could only be concluded that bacteria played an important role in the toxemia of strangulation obstruction. Better sterilization of the bowel was necessary to further evaluate the importance of bacteria.

Additional evidence for the role of bacteria was a study correlating the level of obstruction with the incidence and degree of hemorrhage, necrosis, and ulceration of the intestinal wall in simple obstruction.[26] These abnormalities increased as the level of obstruction progressed down the gastrointestinal tract. This was attributed to increased bacterial growth in the more nearly ideal conditions of obstruction and the lowered resistance of the bowel subsequent to the ischemia of distention.

Part of the failure of penicillin was attributed to the inability to obtain a sufficient antibacterial level in the bowel lumen. It was hoped that the poorly absorbed antibacterial agents might solve this problem. These were first tried in experiments with strangulated but not obstructed bowel. It was repeatedly shown that adequate antibacterial therapy would protect a segment of bowel deprived of its blood supply.[23, 27, 38, 39, 41, 42] Revascularization, studied by radiopaque dye injection, was shown to come from new small vessels running the full length of the mesentery, arcades bridging the divided vessels and restoring their continuity, mesenteric vessels of adjacent loops, adhesions to serosa of healthy loops, and the omentum.[39, 42] Histologic studies showed that the vascular injury alone was not sufficient to render the loops nonviable, but the superimposed bacterial action so aggravated the degree of vascular occlusion as to be responsible for death of the loop and thereby for the death of the animal.[39] No single organism was implicated and it was suggested that bacterial synergism might be necessary to produce the lethal result. It was concluded that bacterial action was a major factor in converting a sublethal to a lethal degree of vascular injury in the dog's bowel.

The use of antibiotics for preoperative sterilization of the bowel has been advocated by numerous surgeons for elective colon surgery. A review of the problem makes it obvious that most workers have their own favorite antibacterial agents.[40] On the basis of a standard clinical and bacteriologic routine for comparing all agents studied, one group has recently selected Achromycin-Neomycin as the most effective bowel antispetic, with Nystatin-Neomycin as the next choice under certain special circumstances.[19, 20, 21]

If bacteria are so important, preoperative sterilization of the gastrointestinal tract, combined with adequate postoperative antibacterial therapy, should improve survival in experimental strangulation obstruction.[14, 15] Dogs were prepared with preoperative oral sulfathalidine and streptomycin or oral Aureomycin. Postoperative antibacterial therapy included intramuscular penicillin and intravenous Aureomycin. Average survival, 71½ hours, was twice the survival obtained in animals that did not receive antibiotics. Cultures of the bowel lumen and of the peritoneal fluid confirmed the value of preoperative intestinal antisepsis. Histologically, there was significantly less destruction in the bowel wall than in those animals that did not receive antibiotics. There was excellent preservation of the mucosal layer, bacteria were rare, and the bowel wall was relatively normal in appearance. Since the use of antibiotics was the only difference in technic from earlier experiments by the same group, the improved survival was attributed to antibiotic suppression of bacterial growth.

Death of some animals could not be explained until later work[32, 33] revealed that intravenous Aureomycin inadvertently had been used in a toxic range throughout these experiments. It was then suggested that if the antibiotics could be administered by a nontoxic route, further benefits might be anticipated.[15]

The use of a plastic tube to introduce antibiotics directly into the lumen of the strangulated bowel seemed to answer this problem.[6, 9] Dogs, prepared with oral Aureomycin, were subjected to the same strangulation obstruction procedure. Postoperatively, Aureomycin was introduced into the strangulated segment by means of the plastic tube which had been threaded into the strangulated segment at surgery. All dogs in this series survived to be reoperated upon at a time of election, when the strangulated segment was resected and intestinal continuity restored. The time selected for reoperation was longer than any previous survival in strangulation obstruction, was at an interval when it did not appear that further observation would be of any benefit, and was selected after a prolonged survival in the first experiment demonstrated that the bowel had already begun to return towards a normal appearance and had thus avoided the possibility of death from strangulation alone. The peritoneal fluid in these animals never changed to the dark, foul-smelling, or hemolyzed fluid observed in the nonantibiotic treated animals and clostridia were not found in the peritoneal fluid. Fluid intake and output were significantly less than those of either the nonantibiotic treated animals or the animals which received postoperative intravenous Aureomycin. The loss of blood into the gastrointestinal tract and the amount of hematemesis were insignificant compared with previous series, although all the reasons for this decrease were not apparent. The finding of a strangulated segment which had retained its viability was an important observation. The strangulated segment was thicker, shorter, and smaller in circumference than normal, due to hemorrhage, edema, and contraction of the muscular wall. The serosal surface showed only some underlying hemorrhage. The mucosal surface was not distinguishable from the immediately adjacent normal mucosa. The reduction in bacterial flora prior to operation and the maintenance of a reduced bacterial flora in the strangulated segment following strangulation must have played a significant role in permitting the mucosa to retain its normal characteristics since the use and method of administration of antibiotics were the only ways in which this series differed from previous series. Even microscopically the strangulated bowel was essentially within normal limits. This demonstrated that dogs with strangulation obstruction can be kept alive indefinitely if the bacterial flora of the bowel can be controlled. The importance of the bacterial phase of toxicity in strangulation obstruction thereby was established.

Comparable results have been obtained without preoperative bowel sterilization.[8, 10] Limiting all antibiotic therapy to the postoperative period circumvented the objection that preoperative antibiotic therapy was of no value in studying the problem since it had no clinical applications. When Achromycin was injected through a plastic tube directly into the strangulated segment in

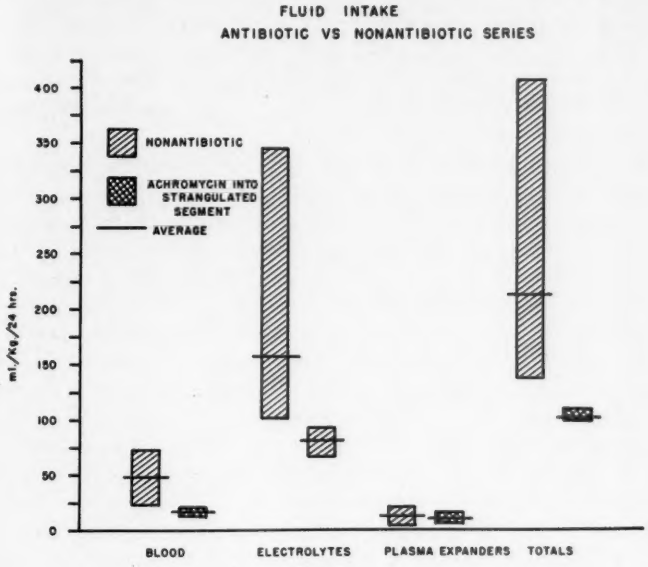

FIG. 1.

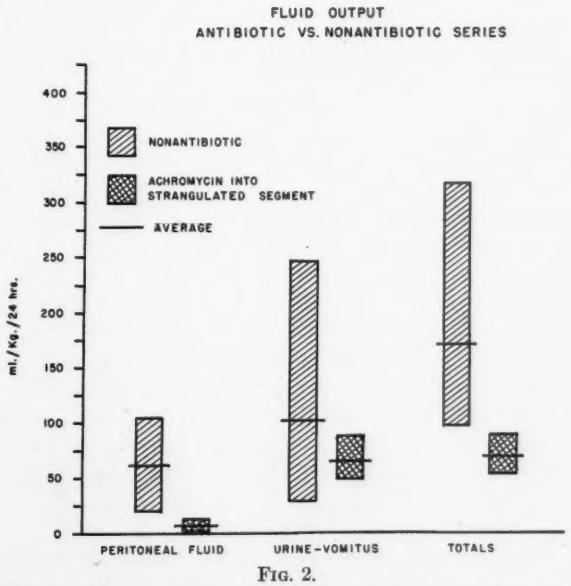

FIG. 2.

FIGS. 1 and 2. Fluid balance comparisons of strangulation obstruction experimental series treated without antibiotics and treated with postoperative antibiotics. Height of bars indicates range of values. Line across bars represents average value.

the postoperative period, all animals survived. This pointed more directly to the time when bacterial control was most important. The normal gross and microscopic appearance of the bowel resected from these animals attested to the value of antibacterial therapy and the importance of bacterial factors in strangulation obstruction.

The correlation of bacterial control and fluid balance studies was an interesting observation.[8, 10] Comparisons between different series of experiments on a ml/Kg/24 hour basis demonstrated that the better the control of the bacterial flora of the bowel, the less the fluid requirements (figures 1 and 2). A partial explanation for these observations is that bacteria in the lumen of the strangulated segment cause loss of fluid into the strangulated bowel and this eventually leads to vomiting. These bacteria also cause bleeding into the bowel lumen by destroying blood vessels in the strangulated segment as total destruction of the bowel wall occurs. This accounts for the greater incidence of hematemesis in the nonantibiotic series and consequently for the increased need for blood. As the bacteria or their toxins pierce the bowel wall, peritoneal exudation becomes severe. These losses are prevented by adequate bacterial control, and replacement requirements thereby are reduced.

Further evidence of the importance of bacterial control has been provided by a study of antibiotic protection of devascularized colon anastomoses.[22] Animals without any preoperative preparation did not survive devascularization of one side of a colon anastomosis while a similar series with postoperative intracolonic antibiotic administration did survive. Results such as this in the colon should make more plausible the reported results in the small bowel with its comparatively small bacterial content.

A new approach to the study of strangulation obstruction has been the use of a Thiry fistula preparation, which avoids many complicating factors that have confused this subject in the past.[7, 11] These studies show that death can occur in the absence of all secretions except those of the fistula, and indicate a close correlation between death of the animals and bacterial content of the fistula at the time of strangulation.

SUMMARY

In an attempt to confine this review to the "*antibiotic era*" it has been necessary to omit much important related work which antedated the antibiotic agents. However, correlation of the older and newer information has been simplified.

The strangulated, obstructed, small bowel presents ideal conditions for the growth of certain anaerobic organisms. The growth of *Cl. welchii* is significantly stimulated under these conditions, and focuses attention upon the activity of these organisms in strangulation obstruction.

Adequate treatment with fluids, electrolytes, blood, and plasma prolongs survival in experimental strangulation obstruction beyond that achieved by any previous methods. Shortly before death, there are significant spectrophotometric, chemical, bacteriologic, and gross changes in the peritoneal fluid. Cul-

tures of the early peritoneal fluid frequently are sterile in contrast to the varied bacterial flora usually found in the later peritoneal fluid. Spectrophotometric studies of a new pigment in strangulation obstruction suggest that the route of absorption of this agent and, presumably, of any other substances is from the bowel lumen, across the bowel wall into the peritoneal cavity, and then into the systemic circulation. Toxicity of the late peritoneal fluid was demonstrated by injecting this fluid directly into normal animals with fatal results. Neither the abnormal spectrophotometric curve nor lethal results have been obtained by any mixtures that completely eliminated bacteria or their products.

There appears to be a better correlation between the bacterial content of the peritoneal fluid and the clinical course of patients with strangulation obstruction, than between the spectrophotometric findings in the peritoneal fluid and the clinical course.

Duodenal, biliary, and pancreatic secretions are not essential for a lethal result in strangulation obstruction.

A close correlation has been observed between the toxins of *Cl. welchii* and the fatal outcome in both experimental peritonitis and strangulation obstruc-

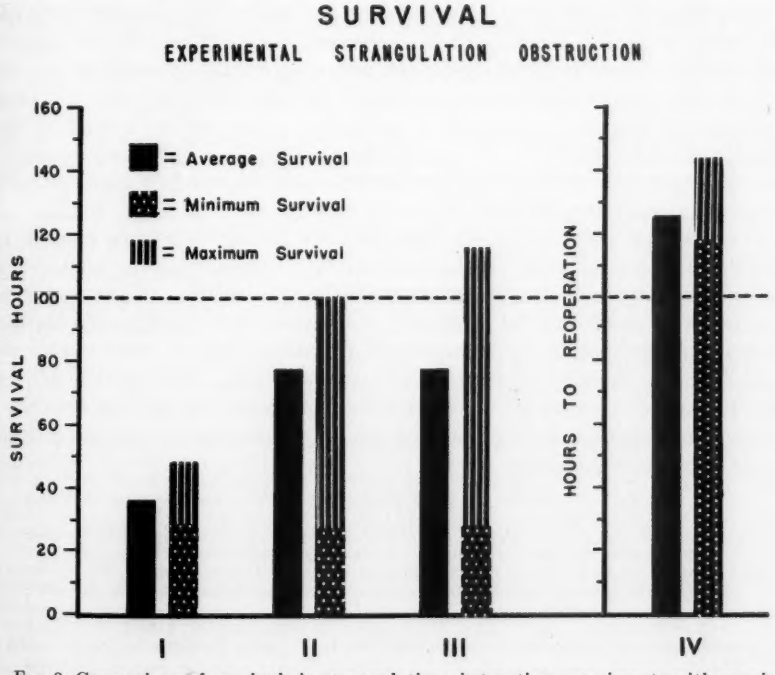

FIG. 3. Comparison of survivals in strangulation obstruction experiments with varying forms of antibacterial therapy. Line at 100 hours indicates time of election for reoperation in series receiving only postoperative intraluminal antibiotics. I. No antibiotics; II. Postoperative penicillin; III. Preoperative antibiotics, postoperative intravenous Aureomycin; IV. Preoperative preparation, postoperative intraluminal Aureomycin.

tion. Sublethal doses of *Cl. welchii* plus sterile segments of bowel in the peritoneal cavity of normal dogs produce a fatal result, although neither of these alone would.

Penicillin significantly prolongs life in strangulation obstruction, although survival still is limited. Orally administered antibacterial agents protect the small bowel of animals with venous strangulation of long segments, while unprotected animals die rapidly. The new circulation comes from the omentum, the mesentery, adhesions to normal bowel, and the wall of the bowel itself.

With proper antibiotic protection, provided by direct injection of antibacterial agents into the strangulated, obstructed bowel, viability of obstructed, strangulated segments of bowel can be maintained, in contrast to the rapid death without antibiotic protection (figure 3). Revascularization of this bowel presumably comes from the same sources as for strangulated but not obstructed bowel. Later resection of such a strangulated segment reveals it has returned essentially to normal grossly and microscopically. Blood loss and fluid requirements are reduced in animals with proper antibacterial protection.

Following strangulation, bacteria are thought to invade the bowel wall, grow, produce toxins, increase vascular permeability, and destroy the bowel wall. During this process, blood loss, hematemesis, and general fluid loss are increased. Permeability of the bowel wall is increased, and gastrointestinal contents permeate the bowel wall to lodge in the peritoneal cavity. Absorption into the systemic circulation after this is responsible for the fatal outcome. Adequate preoperative intestinal antisepsis or adequate postoperative control of the intraluminal bacterial flora will control the bacterial flora sufficiently to permit the body's normal defenses to combat bacterial activity and thus regain viability for the strangulated segment.

Even though antibiotics have been used to provide indefinite survival in experimental strangulation obstruction and thus demonstrate the vital role of bacteria in the cause of death in strangulation obstruction, this must not be interpreted to mean that the treatment of a patient with strangulation obstruction should be limited to antibacterial measures. Surgery still remains the major form of therapy for patients with this condition, but experimental evidence obtained with the aid of antibacterial agents has brought one step closer the eventual solution of the problem of the role of bacteria in the cause of death in strangulation obstruction.

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SURGICAL TREATMENT OF CANCER OF THE THYROID

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Many reports have been made on the surgery of nontoxic nodular goitre. From an analysis of even a small part of the published material, it quickly becomes apparent that the clinical differentiation between benign and malignant nodules is exceedingly difficult. Because of this difficulty, the predominant belief among members of the surgical staff of the Roosevelt Hospital has long been that all nodular goitres should be removed and submitted to microscopic study.

In recent years the operative management of the less malignant tumors of the thyroid has become somewhat controversial.[5, 10] Some surgeons believe in an essentially conservative operation, consisting of partial or total removal of the involved lobe and local removal of any lymph node metastases. This belief arises from the observation that certain histologic types of this disease usually run a prolonged course, while others may prove rapidly fatal regardless of how radical the treatment may be. Opposing this group are those who advocate radical neck dissection with removal of the involved lobe and isthmus in all thyroid cancer, wherever such a procedure is feasible. This more radical approach is used principally in institutions that specialize in the treatment of cancer and is based, in part, on the fact that approximately 40 per cent of the patients referred to them are what they term "treatment failures". Treatment involved in these failures "has included subtotal thyroidectomy with or without irradiation, thyroidectomy with neck dissection, biopsy with irradiation, or irradiation only".[4] A second reason given for performing the radical operation is the fact that in radical neck dissection for papillary thyroid cancer, 61 per cent of the patients were found to have local lymph node involvement despite the absence of clinically demonstrable lymph node metastases.[8]

The existing controversy cannot be settled in the immediate future because the slow growth of the less malignant types of thyroid tumors necessitates a long follow-up of patients treated by one or the other method. In the meantime, the general surgeon is left in somewhat of a quandry. It is unlikely that he will see enough cases in his lifetime to enable him to determine the relative merits of each approach.

At the Roosevelt Hospital, surgery has generally been of the more conservative type. In order to determine the soundness of our attitude, the cases of all patients who had thyroid cancer and were treated on the Surgical Services during the past 25 years have been reviewed.

* From the Roosevelt Hospital, New York City.

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MATERIAL

Ninety-one histologically proved thyroid cancers were treated during the 25 year period from 1930 to 1955. Six patients could not be traced following discharge from the hospital. The remaining 85 have been followed for periods up to 23 years. Eight patients were admitted with histologic diagnosis already established elsewhere. The 91 patients were operated upon by 20 different attending surgeons and a number of residents. Because of the fact that we have had no inflexible policy about the management of these problems, the extent of operation has varied with the attitude of the surgeon in charge.

ANALYSIS OF CASES

Incidence: Eighty-nine thyroid cancers were encountered in 1131 operations for nodular goitre, giving an incidence of 7.8 per cent. In 2 patients, a focus of carcinoma was accidentally found during bilateral subtotal thyroidectomy for diffuse hyperthyroidism.

Age and Sex: The average age of the 91 cancer patients was 47 years, the youngest being 10 years old and the oldest 84. Six patients were under 20 years of age. Of the entire series, 68 per cent were between the ages of 31 and 60 at the time of operation.

There were 71 (78 per cent) females and 20 (22 per cent) males in the series. Both the average age and the ratio of males to females closely parallel those given in reports from other institutions.

Duration of Nodule: Little significant information could be obtained as to the relationship between the duration of the nodule and the presence of cancer. In 3 instances, the nodule was first observed on routine examination, the patient being unaware of its existence at the time. One patient had been aware of the nodule for 49 years.

The pathologic reports did not provide conclusive evidence that these cancers arose in pre-existing adenomas. We are inclined to agree with Martin[10] that "although some thyroid cancer does arise in pre-existing adenomas, it has also been abundantly established that thyroid cancer can arise independently in non-neoplastic thyroid tissue".

Clinical Manifestations: Seven patients were admitted with a clinical diagnosis of hyperthyroidism, 5 with toxic nodular goitre, and 2 with toxic diffuse goitre. In the last 2 patients, basal metabolic rates were +39 and +67, respectively. The diagnosis of hyperthyroidism was confirmed in the pathologic laboratory and the presence of cancer was an unexpected finding. Three other patients had had fairly recent surgery for hyperthyroidism, 2 for toxic diffuse goitre, and one for toxic nodular goitre. Carcinoma had appeared in the 2 patients with diffuse goitre 1 and 4 years respectively after the operation, and 2 years later in the patient with toxic nodular goitre. It is conceivable that the cancers in this group, all of the less malignant type, were present at the original operation. In this series, the association of cancer and hyperthyroidism is 7.7 per cent. Cole[2] notes an association of 9 per cent in his series, but considers the occurrence of cancer in diffuse toxic goitre highly unlikely.

Eight patients complained of hoarseness, 2 of dysphagia, and 3 of pressure

in the throat. Five complained of the slow growth of a lump in the neck, and one of the rapid growth of a lump. Horner's syndrome was present in one patient. Only one patient was admitted for the treatment of what proved to be a distant metastasis of a thyroid tumor. In all the other patients, the principal clinical manifestation was a mass in the neck.

DIAGNOSIS

From our experience, we believe that the clinical diagnosis of cancer of the thyroid is exceedingly difficult. For many years, the solitary tumor of the thyroid has been generally accepted as the tumor most likely to prove malignant. Many reports cite an incidence of malignancy varying from 10 per cent to 24 per cent in solitary nodules, and .62 per cent to 7.5 per cent in multiple nodules. In pathologically proved solitary tumors, Martin[10] found an 8 per cent incidence of cancer, while in multinodular goitres the incidence was 15 per cent. He also found that the members of the Head and Neck Service of the Memorial Hospital had made a 24 per cent error in the clinical diagnosis of single and multiple nodules. Allowing for this error, Martin thought that in a clinical diagnosis of a solitary tumor there was a 10 per cent chance of cancer, and in the case of a multinodular goitre, there was a 12.5 per cent chance.

At Roosevelt Hospital, because of our past experience, we believe that all nodules in the thyroid gland should be viewed with extreme suspicion and regarded as possibly malignant, and that a definite diagnosis cannot be made without the aid of the microscope. Such signs as palpable nodules in the jugular chain, hoarseness, Horner's syndrome, pulmonary symptoms, or distant bony metastases in the presence of a tumor of the thyroid gland obviously facilitate the diagnosis. Although aspiration biopsy is occasionally of value in establishing the diagnosis, there always is the risk of missing the cancer entirely. Martin[10] uses this technic only in doubtful cases. One observer has reported the case of a patient in whom a distressing complication developed, with tumor cells growing at the site of aspiration.[4]

The difficulty of making a preoperative diagnosis of thyroid cancer is attested by reports from various clinics. Cole[3] reported a diagnosis of 21 per cent before operation, 21 per cent at operation, and 58 per cent in the laboratory. The Ochsner Clinic[1] reported, in the same order, percentages of 36.6, 24, and 39.

In this series, there was a positive diagnosis in 38 per cent before operation (including 10 per cent before admission), 20 per cent at operation, and 42 per cent in the laboratory. The clinical accuracy of 92 per cent reported by Crile[4] has not been equalled in any other published report.

PATHOLOGY

No completely satisfactory histologic classification of thyroid cancer has yet been developed. Because of the finding of 15 different histologic types in this series of 91 cases, the pathologic material was reviewed and re-classified in accordance with a modification of Warren's method.[11] His classification is one of the most simple to use and is becoming more generally adopted.

In recent years, some doubt has been cast on the need of including the so-

TABLE I

Histologic classification of 91 patients with thyroid cancer treated at the Roosevelt Hospital, 1930–1955

Type	No. of Cases	Per Cent
Papillary adenocarcinoma	38	42
Follicular and alveolar adenocarcinoma	23	25
Hurthle cell carcinoma	9	10
Solid adenocarcinoma	7	8
Giant and spindle cell carcinoma	10	11
Sarcoma	4	4
Total	91	100

called "Hurthle cell adenocarcinoma" in the classification. Horn[9] has concluded that "cancers composed of Hurthle cells are readily segregated according to the classifications for thyroid tumor in which Hurthle cells do not form a conspicuous component, and that the degree of clinical malignancy corresponds to that of the various usual types of thyroid carcinoma".

The histologic classification of our 91 cases of proved thyroid cancer is shown in table I.

The incidence of papillary carcinoma is 42 per cent, which is somewhat lower than that encountered in other clinics. In 1949, Frazell and Foote[7] reported an incidence of 46 per cent at Memorial Hospital, and this figure is now reported to be approaching 60 per cent.[6] Cerise, Randall and Ochsner[1] reported, in 1952, an incidence of 56 per cent. The sudden general increase in the incidence of papillary adenocarcinoma might also be confirmed by our findings, since 43 per cent of our patients have been operated upon in the last 5 years.

With regard to our follicular and alveolar adenocarcinoma cases, we cannot account for the fact that the incidence we experienced was almost twice that reported in other studies. Nor can we account for our incidence of solid carcinoma, which is half of that reported by other investigators. The incidence of Hurthle cell adenocarcinoma and spindle and giant cell carcinoma among our patients approximates that reported by other investigators.

TREATMENT

Although the clinical course of an individual case of thyroid cancer is quite unpredictable, the natural history of the various types follows a fairly consistent pattern. This point is often not stressed in reports dealing with over-all results of the treatment of all types of thyroid cancer.

Papillary Cancer: The following operations were performed on 38 patients:

Unilateral subtotal thyroidectomy	15 cases
Bilateral subtotal thyroidectomy	4
Lobectomy	6
Primary radical neck dissection	2
Secondary radical neck dissection	3

Biopsy and subtotal thyroidectomy	4
Decompression	1
Lobectomy and modified neck dissection	3

Among those patients treated by unilateral subtotal thyroidectomy, 2 have died of recurrence of the disease. (Both of these patients were operated upon in 1940.) One developed disease in the trachea 2 years following the primary operation and died a year later. The second had multiple excisions of local recurrences during the remaining 8 years of her life.

In the group treated by lobectomy and modified neck dissection, there was one death 7 years after the primary operation. The original procedure in this patient was a total removal of the right lobe, isthmus, and part of the left lobe. Seven months postoperatively, lymph node involvement appeared on the left side, necessitating a left radical neck dissection. Nine months thereafter, a right radical neck dissection was performed. Thirty-nine months later, it was necessary to perform tracheotomy and partial removal of the sternum because of disease in the mediastinum. Two years later, the patient died of distant metastases.

In 3 other patients in the entire group of papillary cancer, secondary operations were performed in an attempt to control their disease. In one patient, the cancer was finally controlled by x-ray therapy and she has been without clinical evidence of disease for 5 years. In the second patient, disease was controlled by radioactive iodine after 3 excisions for local recurrences, during the first 3 years after the original operation. The third patient had a local excision of a recurrence in the mastoid area 2 years after lobectomy.

Follow-up: Of the 38 patients in this group, one with papillary adenocarcinoma died immediately after operation. This was the only operative fatality in the entire series of 91. Five patients have been lost to follow-up, of whom 4 were without clinical evidence of disease when last seen. The fifth patient, whose attending surgeon thought that the primary operation was inadequate, refused radical neck dissection. Thirty-three of the patients (87 per cent) have been observed for periods up to 23 years. The following table summarizes the results in this group.

Patients Followed	<5 yrs.	5–10 yrs.	10–15 yrs.	15 yrs.+
Alive without disease	10	6	4	5
Alive with disease	1			
Dead of disease	1	2		
Dead of other causes	1	1	1	1

In addition to the 3 patients who died of the disease, 3 are known to have died of other causes. One died of a cerebrovascular accident, proved at autopsy, 5 years after operation. Incidentally, asymptomatic disease was found in the mediastinum at that time. Death in 2 other patients, 14 and 22 years after operation, was due to coronary occlusion, proved at autopsy in both.

Twenty patients (61 per cent) have been followed for a period of 5 years or

longer. Since 2 of these are now dead of thyroid cancer, this provides another example of the inadequacy of 5-year survival rates in the evaluation of treatment of this disease. Although 25 of our 33 patients are free of disease, including 15 observed more than 5 years, we are in agreement with Frazell[7] that as these patients are followed for periods well beyond 5 years, more deaths from recurrences will probably occur.

Follicular and Alveolar Adenocarcinoma: The following operations were performed in 23 patients:

Unilateral subtotal thyroidectomy	8 cases
Bilateral subtotal thyroidectomy	6
Lobectomy	4
Lobectomy and modified neck dissection	2
Biopsy and x-ray	2
Local excision of recurrences	1

Of the 6 bilateral subtotal thyroidectomies performed, 4 were done for hyperthyroidism and 2 for bilateral disease. One of the hyperthyroid patients died 2 years after operation of a leiomyosarcoma of the abdominal cavity. Another died 5 years after operation, with exact cause unknown. A small circumscribed focus of disease buried in the substance of the lobe had been found at the primary operation of this last patient. She had been seen in the Thyroid Clinic 2 months before her death, and at that time clinical examination had failed to show evidence of disease. One patient with bilateral disease died 1½ years later of a hemorrhage into the trachea, a portion of which had been removed at the primary operation.

One patient who underwent lobectomy had had two previous operations for hyperthyroidism. Two years after the second operation, a nodule appeared which proved to be malignant on excision. She died 1 year later. The 2 patients treated by simple biopsy and radiotherapy because of inoperable cancer both died of disease within 2 years.

Two other patients in this group underwent secondary local excisions for recurrent disease in the neck. One of these was subsequently referred elsewhere for radioactive iodine therapy and has since been lost to follow-up at both institutions. The second patient has been without evidence of disease for 6 years after the second recurrence and for 23 years after her primary operation elsewhere.

Follow-up: The following table summarizes the postoperative observation of 22 patients of this group.

Patients Followed	<5 yrs.	5–10 yrs.	10–15 yrs.
Alive without disease	9	6	1
Dead of disease	4		
Dead of other causes	1	1	

One patient was lost to follow-up after discharge from the hospital. The longest follow-up was 13 years. With only 36 per cent of these patients fol-

lowed for 5 years or longer, the known death rate of 18 per cent will probably increase.

Hurthle Cell Carcinoma: The table below summarizes the treatment in 9 patients:

Unilateral subtotal thyroidectomy	7 cases
Biopsy and x-ray	1
Local excision and x-ray	1

The biopsy was performed in the presence of generalized metastases and the patient died 2 months later. The local excision was done for a recurrence in a patient who had had 3 previous operations elsewhere during the preceding 9 years. This same patient received 2 courses of x-ray treatment. Death occurred 13 years after the primary operation.

Follow-up: The postoperative record of this group of 9 patients, one of whom died of senility 14 years after operation, is as follows:

Patients Followed	<5 yrs.	5–10 yrs.	10–15 yrs.
Alive without disease	6		
Dead of disease	1		1
Dead of other causes			1

As mentioned earlier, there is strong evidence that Hurthle cell cancers conform to the clinical course of other thyroid cancers where this type of cell is not predominant. This small series, followed for so short a time, does not justify any conclusions.

Solid Adenocarcinoma: The procedures carried out on 7 patients in this group were as follows:

Unilateral subtotal thyroidectomy	1 case(s)
Biopsy	1
Decompression	2
Radium and x-ray	2
Local excision	1

Only 2 of the 7 patients were treated at the Roosevelt Hospital originally. One had a unilateral subtotal thyroidectomy and is alive without evidence of disease 6 years after operation. The other, during a stay at the Hospital for gastrointestinal investigation, had a biopsy of what was thought to be Virchow's node. Thyroidectomy was refused. He died of disease 10 years later in another hospital, still without having submitted to thyroidectomy. The other 5 patients received palliative treatment.

Follow-up: The late results in this group are as follows:

Patients Followed	<5 yrs.	5–10 yrs.	10–15 yrs.
Alive without disease		1	
Dead of disease	5		1

Giant and Spindle Cell Carcinoma: The 10 patients in this group were treated by the following procedures:

Lobectomy and local excision of involved nodes	1 case(s)
Lobectomy	3
Decompression	3
Biopsy and x-ray	2
Excision of metastases	1

The patient treated by lobectomy and excision of the chain of nodes along the jugular vein had one node involved on the opposite side, which also was excised. This patient is alive 11 years after operation, having subsequently had 3 local excisions for recurrences and a radical neck dissection on the opposite side, in addition to numerous courses of x-ray therapy. She now is in another institution receiving radioactive iodine for recurrent disease.

The 3 lobectomy patients were not subjected to further surgery because of disease invading the trachea, larynx or esophagus. The patient in whom a distant metastasis was excised at the primary operation was found to have an unrecognized carcinoma of the thyroid at autopsy.

Follow-up: The results in this group of 10 patients were as follows:

Patients Followed	<5 yrs.	5–10 yrs.	10–15 yrs.
Alive with disease			1
Dead of disease	9		

Sarcoma: Since sarcoma in the thyroid gland is primarily a manifestation of systemic disease, it is questionable that it should be included in a classification of thyroid cancer. However, it does present a problem to the surgeon at the operating table, principally because the differentiation by frozen section between lymphosarcoma and Hashimoto's disease is exceedingly difficult. In 3 cases of lymphosarcoma and one of Hodgkin's disease, subtotal thyroidectomy as would be expected, had no effect on the course of the disease.

COMMENT

Table II summarizes the operative procedures performed on 91 thyroid patients.

Although the procedures employed by different members of our surgical staff varied somewhat, most of these 91 patients were treated by lobectomy or subtotal thyroidectomy without neck dissection.

Table III summarizes the follow-up on 85 of the 91 patients:

No decisive conclusions can be reached since 30 per cent of the patients had been followed for less than 5 years. While the average survival, without evidence of recurrence, for the entire group was 56.7 per cent, the rate varied in the different types of tumor. Certain tumors were obviously more lethal than others. In the 24 patients (86 per cent) who died in less than 5 years after surgery, 80 per cent had the more malignant types of thyroid cancer. Fifty per cent of these 24 deaths occurred in patients who received only palliative treatment.

TABLE II

Surgical procedures for cancer of the thyroid, 91 cases treated at Roosevelt Hospital, 1930–1955

Procedures	Diagnosis						Total Cases
	Adenocarcinoma			Carcinoma		Sarcoma	
	Papillary	Follicular and alveolar	Solid	Hurthle cell	Giant and spindle cell		
Unilateral subtotal thyroidectomy	15	8	1	7	—	1	32
Bilateral subtotal thyroidectomy	4	6	—	—	—	3	13
Biopsy and subtotal thyroidectomy	4	—	—	—	—	—	4
Lobectomy	6	4	—	—	3	—	13
Lobectomy and modified neck dissection	3	2	—	—	1	—	6
Primary radical neck dissection	2	—	—	—	—	—	2
Secondary radical neck dissection	3	—	—	—	—	—	3
Decompression	1	—	2	—	3	—	6
Local excision of recurrence	—	1	1	—	—	—	2
Excision of metastasis	—	—	—	—	1	—	1
Local excision and x-ray	—	—	—	1	—	—	1
Biopsy	—	—	1	—	—	—	1
Biopsy and x-ray	—	2	—	1	2	—	5
Radium and x-ray	—	—	2	—	—	—	2
Total	38	23	7	9	10	4	91

TABLE III

Follow-up of 85 patients with cancer of the thyroid treated at Roosevelt Hospital, 1930–1955

Patients Followed	Years of Observation				Total	
	<5	5–10	10–15	15 or more	Cases	Per cent
Alive without disease	25	13	5	5	48	56.7
Alive with disease	1	—	1	—	2	2.3
Dead of disease	24	2	2	—	28	32.8
Dead of other causes	2	2	2	1	7	8.2
Total	52	17	10	6	85	100.0

The procedures described have thus far produced good results in papillary adenocarcinoma, with only 6 recurrences among 33 patients followed. Results were fair in the follicular and alveolar and in the Hurthle cell cases, where recurrences were respectively 6 among 23 and 2 among 9. In the giant and spindle cell, and in the solid adenocarcinoma cases, results were poor, with only one survivor in each group.

SUMMARY

During the past 25 years, 91 patients with thyroid cancer have been treated on the Surgical Services of Roosevelt Hospital. A comprehensive review of all these cases was made and the current status of 85 was determined. Six patients could not be traced.

Among 38 patients with *papillary adenocarcinoma* who were treated by conservative operation and followed from 1 to 23 years, three (7.8 per cent) are known to have died of thyroid cancer. Of these patients, 61 per cent survived 5 years or more. Two of the deaths occurred 7 years after primary operation.

Among 23 cases with the diagnosis of *follicular and alveolar adenocarinoma*, 4 patients have died (18 per cent). This includes 3 patients in whom the disease was far advanced at the time of surgery. One patient was lost to follow-up.

There were 2 deaths among 9 patients with *Hurthle cell carcinoma*, giving a mortality rate of 22 per cent. One patient died 13 years after the primary operation. The other had generalized metastases at the time of operation and died 2 months later.

Among 7 patients with *solid adenocarcinoma*, 5 were in advanced stages of the disease and received palliative treatment only. Six of the 7 died, giving a mortality rate of 85 per cent.

Of 10 patients with *giant and spindle cell carcinoma*, 9 died within 18 months. One is still alive, despite numerous recurrences during the past 11 years.

Sarcoma in the thyroid gland, in 4 patients, was uniformly fatal in a short period of time.

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HYPOTHERMIA IN HYPERTHYROIDISM: A CASE REPORT

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A physician always hesitates to report a single case. However, from a single case, experiment or operation, valuable observations may be made and a great deal learned. In the case I wish to report the mistakes are enlightening, as well, and it is with the hope that our mistakes and observations may be of value to others that we report this case.

Hyperthyroidism is, in itself, a fascinating subject to the internist and surgeon. However, it is a subject which has been thoroughly covered in the literature by a host of capable authors and it is not the purpose of this paper to attempt to add to the general subject. There are many complications such as the occasional toxic thyroid which cannot be brought to a euthyroid state, or, worse yet, gets out of control while under treatment. This becomes one of the most challenging problems we can be confronted with. Such is the case I wish to present.

CASE REPORT

This patient was a 38 year old white male who first noted symptoms of heat intolerance, irritability and increased appetite in May of 1954. These symptoms gradually increased in severity and, in addition, there was a weight loss of 10 pounds and general fatigability, with quadriceps weakness when I first saw him for this condition on Oct. 20, 1954.

At this time the only significant physical findings were a diffuse enlargement of the isthmus and the lower pole of the right lobe; pulse 120 while sitting; blood pressure 146/90; fine tremor of the fingers; smooth, velvety skin and definite widening of the palpebral fissures.

He was placed on "*Itrumil*" (a Ciba product containing iodine and propylthiouracil) mg. 100 four times a day, and Phenobarbital gr. ½ four times a day, and instructed to eat a hi-caloric diet and have adequate rest. Under this regime he showed rapid, prompt improvement. By November 5 his pulse was 78, blood pressure 126/80, heat tolerance was normal and there was marked decrease in irritability and he had gained 4 pounds. His dosage of Itrumil and Phenobarbital were both reduced and the patient was informed that now was the time to have surgery. This he flatly refused, although urged by both the internist and me to have it done at that time. I realized there was considerable economic pressure and believed that he might change his mind and submit to surgery in a few weeks or months. That was Mistake No. I. This I promptly followed with No. II. Instead of changing his medication, it was simply reduced to mg. 100 twice a day and he was told to report at regular intervals for a check-up. He did once, and was continuing normally. However, on Dec. 3, 1954 when he reported, his pulse was 98. He had stopped gaining and "*didn't feel as well.*" His dosage was put up to Itrumil 100 mg. four times a day and Phenobarbital gr. ½ four times a day, and he was again urged to enter the hospital. He refused, saying he was leaving on a two weeks vacation. He did not report again until January 14 at which time he was obviously worse. His pulse was 108, he was more irritable and tired easily. He now agreed to hospitalization the next day, so his Itrumil was increased to 1000 mg. per 24 hours in divided doses.

Scientific paper read by title during the Tucson Assembly of The Southwestern Surgical Congress, April 16–18, 1956, Tucson, Arizona.

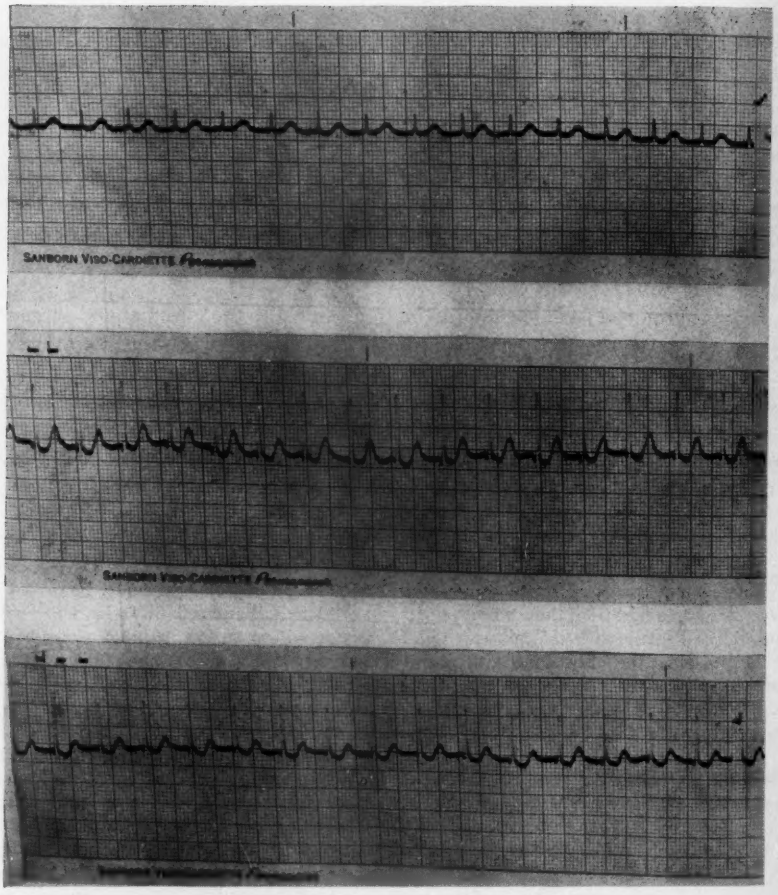

FIG. 1. Initial tracing showing leads I, II, III

He did not enter the hospital until Jan. 19, 1955. Then I made Mistake No. III. He was placed on Lugols solution gtts. 10, three times a day with appropriate sedation. At this point he was extremely toxic with a pulse of 132, and his basal metabolic rate was plus 55 under standardized conditions. His electrocardiogram showed toxic changes (fig. 1).

He was kept on this regime for 4 days before I realized he was iodine fast. Uptake studies now were usless as would be the use of radioactive iodine. Absolute rest and Phenobarbital gr. 1½ every four hours plus Tuinal gr. 3 at bed time and occasional intramuscular sodium luminal were employed. "*Purodigin*" was used up to 0.2 mg. every day. As an antithyroid drug "*Tapizole*" mg. 15, every four hours was used and the patient consumed an average of 6000 to 6500 calories per 24 hours. Oxygen therapy was used but seemed not to influence his course materially, so was discontinued.

Under this regime his basal metabolic rate started to come down slowly and was plus 46 on February 2 and plus 38 on February 14, but he did not gain in weight.

At this point, after additional consultation, a course of deep therapy was given to the thyroid. Improvement, if at all, seemed minimal and we seemed to have hit a *"plateau"*—in fact, a basal metabolic rate on February 21, was plus 45, up 7 points from the last one. Hospitalization could not be dragged out indefinitely and it was believed that some limited surgical procedure, such as polar ligation, or a stage thyroidectomy should be tried.

I had considered using hypothermia for some time with this case. As Bigelow[2], a pioneer in the use and development of hypothermia notes, there is a marked reduction in the metabolic rate with lowered body temperature and oxygen consumption is decreased dramatically. Oxygen consumption studies by him show that oxygen demand is lowered to 50 per cent at 28 C. (83 F.) and to 15 per cent of normal at 20 C. (68 F). Developing this principle, Bigelow[2], Scott[3], Swan [4, 5], Bailey[1] and a host of others have used hypothermia widely in intracardiac and cardiovascular surgery, opening a whole new field in surgery. To date I have read no reports of the use of hypothermia in the United States in the surgical treatment of hyperthyroidism, although a form is used widely in Europe.

This case seemed made to order and, in fact, it seemed an absolute necessity to do something to lower the metabolic rate before any surgery could be attempted. On March 3 he was given a small dose of pentothal in the room on the pretext of drawing another blood for blood chemistry—just our version of the old *"sneak"* tactics used in toxic cases. He was taken to the operating room and his pulse was 86. Only enough anesthesia was used to make intubation possible. The slight manipulation necessary to pass the endotracheal tube shot

FIG. 2. Beginning ice pack

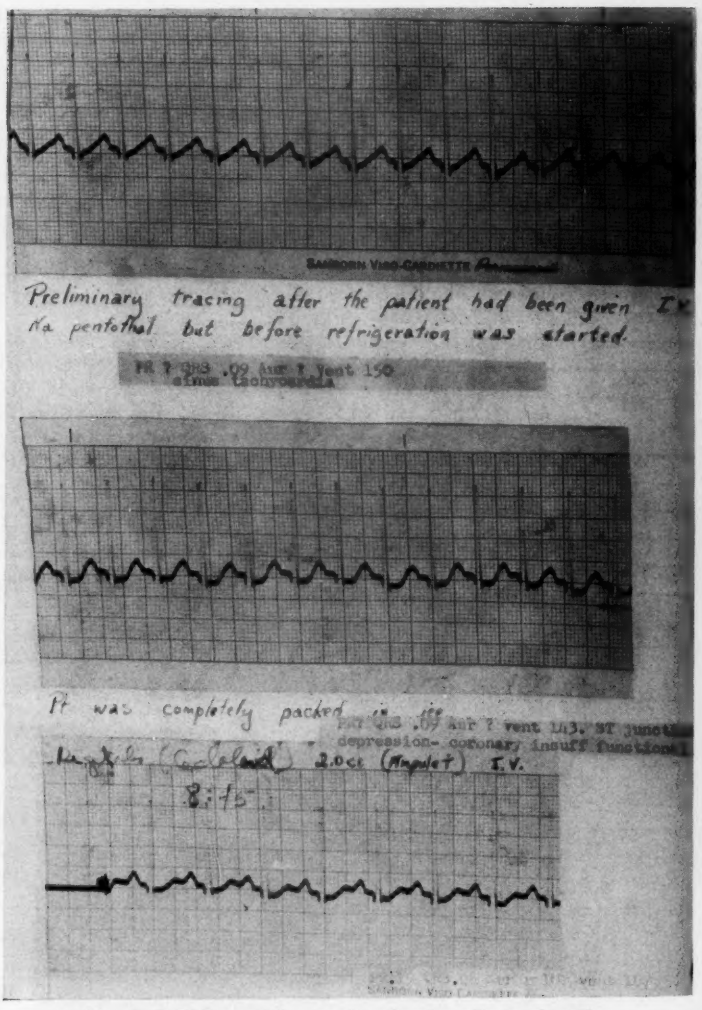
Preliminary tracing after the patient had been given I.V.
Na pentothal but before refrigeration was started.
It was completely packed in ice
2.0cc (Amplet) I.V.

FIG. 3. Initial operative tracing showing effects of cooling

the pulse to 164. Electrodes were attached so that continuous electrocardiographic tracings might be run and the body was thoroughly oiled and wrapped in cotton blankets after inserting the special rectal thermometer used in hypothermia. He then was placed in a cracked-ice pack and cooled to 88 F. (fig. 2, 3, 4). Because of simplicity of equipment, we prefer the ice pack to the tub used by many.

It was assumed that the average additional fall of 3 to 5° would take place. This was Mistake No. IV, for his temperature eventually reached a low of 77, about 8° lower than we desired as an optimum.

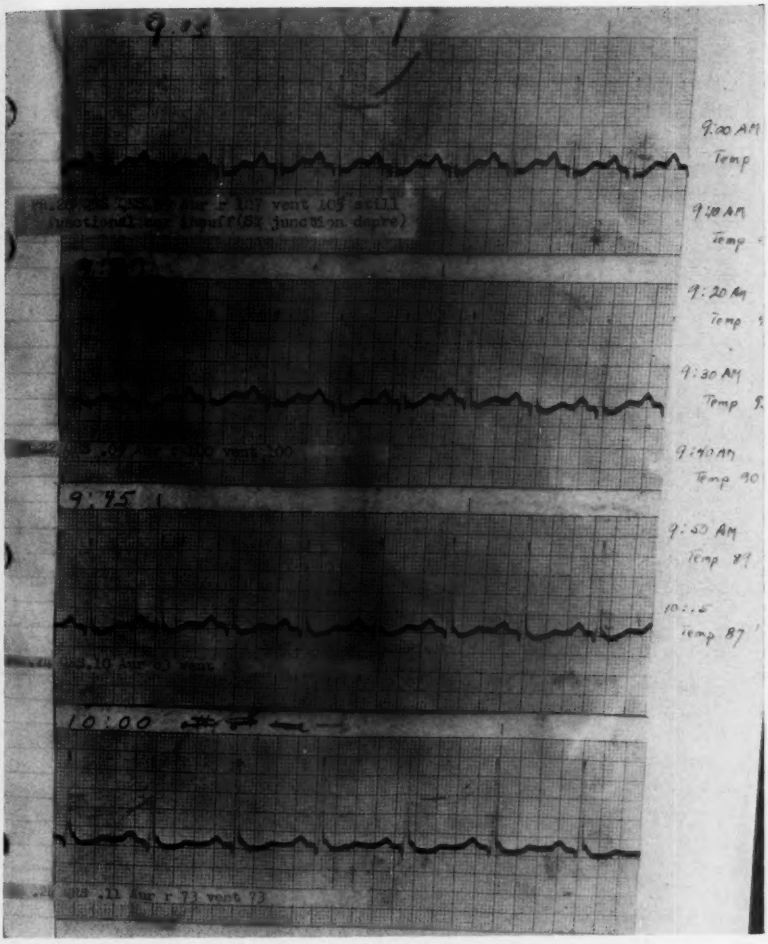

FIG. 4. Additional effects of cooling

After removing the patient from the ice at 88°, the usual preparation was carried out. He was prepped and draped, and collar incision was made. As cooling proceeded there was a widening of the Q.R.S. complex (Fig. 5, 6) At this point external heat was applied in the form of tested, covered hot water bottles to the flanks and thighs. As soon as any manipulation of the thyroid was started, ventricular fibrillation began. Surgery was stopped and the fibrillation did not improve and the heart stopped as shown in figure 8.

The chest was promptly opened and cardiac massage with appropriate intracardiac and intravenous medications restored, after 19 minutes, a rhythm that we considered safe to continue surgery (fig. 9, 10, 11).

With a minimum of manipulation polar ligation was carried out on one lobe. It was noted there was a slight improvement after this, so excision of 9/10 of the left lobe was carried out.

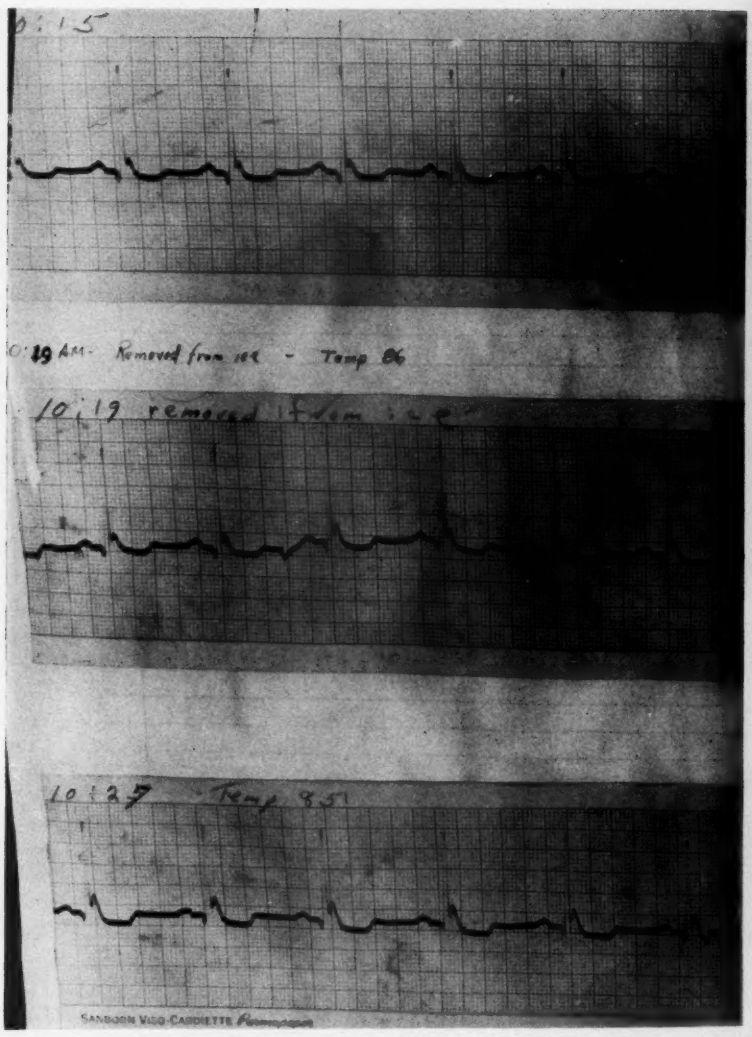

FIG. 5. Slowing of the heart. Shows progressive widening of the QRS complex

There was even more improvement, so we continued to a similar staged procedure on the right side.

This was one of the most interesting observations of the case—that as progressively more and more thyroid was blocked from the circulation or removed, there was a noticeable improvement in the quality of the pulse and electrocardiographic tracings.

After completion of the thyroidectomy, the chest was closed in routine fashion with closed drainage. It was found that there were two areas of second degree burns on the medial

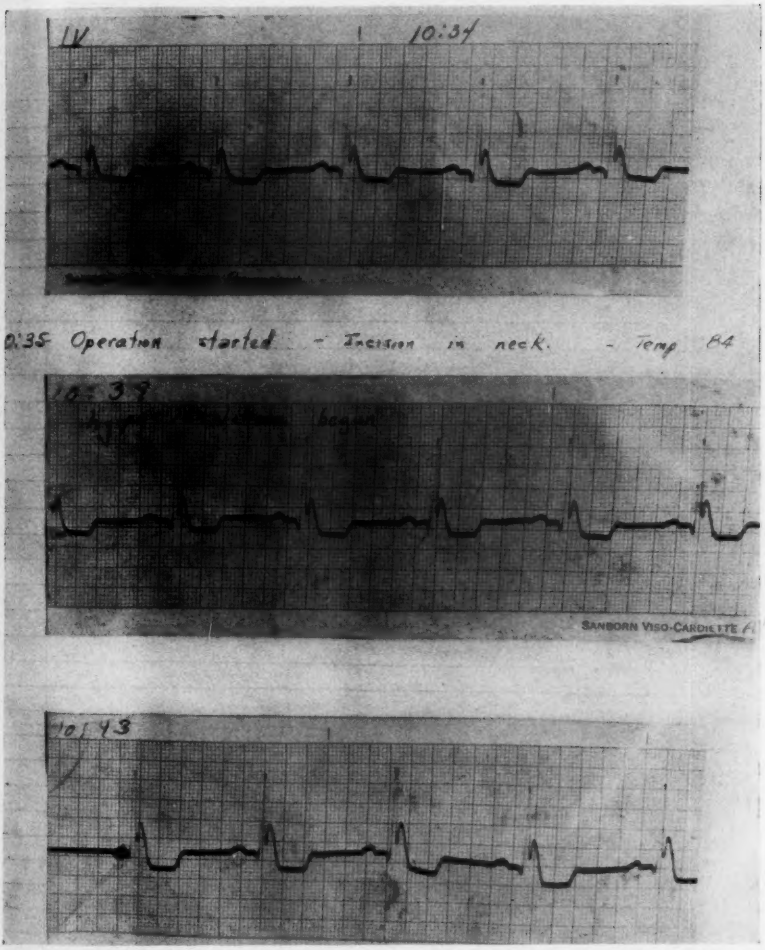

FIG. 6. Further widening of the QRS with depression of the ST segment probably associated with anoxia.

aspect of the thighs where external heat had been applied. These areas were promptly dressed. Blankets and diathermy were applied until his temperature reached 90 F. when only blankets were used.

After the patient's temperature reached 96 F. he was taken to his room and placed in an oxygen tent. He was conscious that evening, out of O_2 in 36 hours and his highest postoperative temperature was 100 F.

Another interesting observation was the marked exophthalmous that began to develop within 24 hours. Reasoning this was due to the sudden withdrawal of thyroxin, the patient was placed on thyroid extract gr. xii by mouth—in divided doses. This was only a guess on the basis of how toxic the patient had been, but proved to be about right for the exophthal-

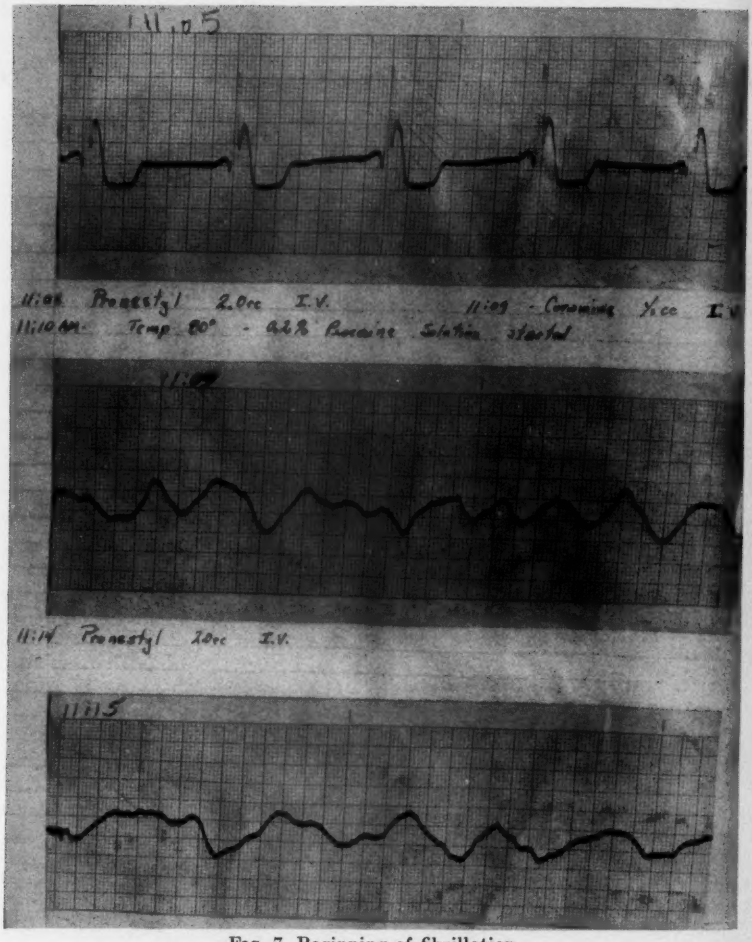

FIG. 7. Beginning of fibrillation

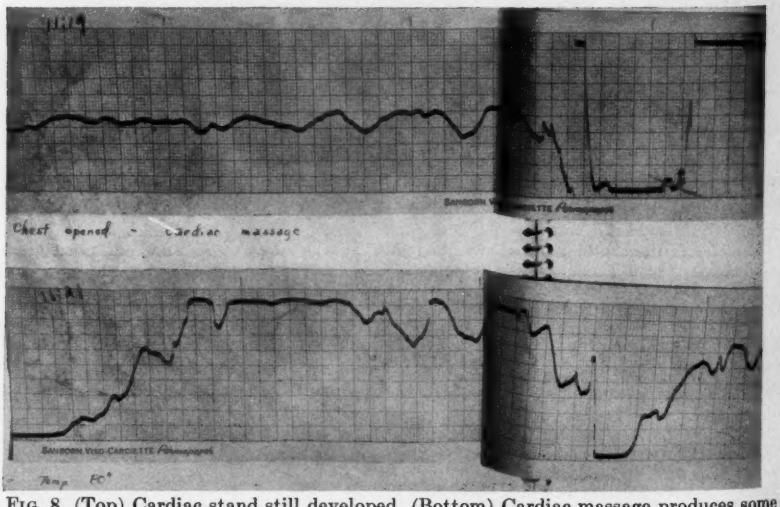

FIG. 8. (Top) Cardiac stand still developed. (Bottom) Cardiac massage produces some fibrillation.

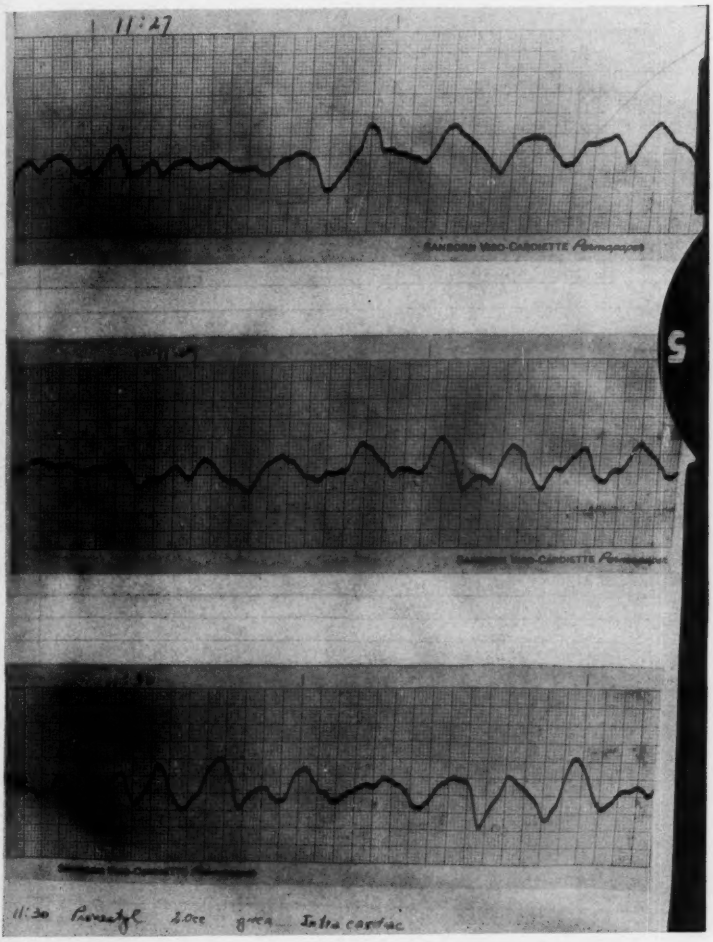

FIG. 9. Cardiac massage continued. No definite rhythm

mous disappeared almost dramatically and did not reappear. Thyroid was cut gradually and discontinued entirely on the fourteenth postoperative day.

Upon leaving the hospital March 31, 1955, the seventy-first hospital day, the pulse was averaging in the low eighties, temperature was normal and the patient was slowly but steadily gaining strength. His electrocardiogram was essentially normal and while his check basal metabolic rate was up to a plus 19, the large amounts of thyroid may have been a factor.

This patient has been checked at regular intervals in the office since. He was last seen March 7, 1956. His pulse averages in the seventies. He regained his strength and weight rapidly and started back to part-time work as a parts man in an implement house on April

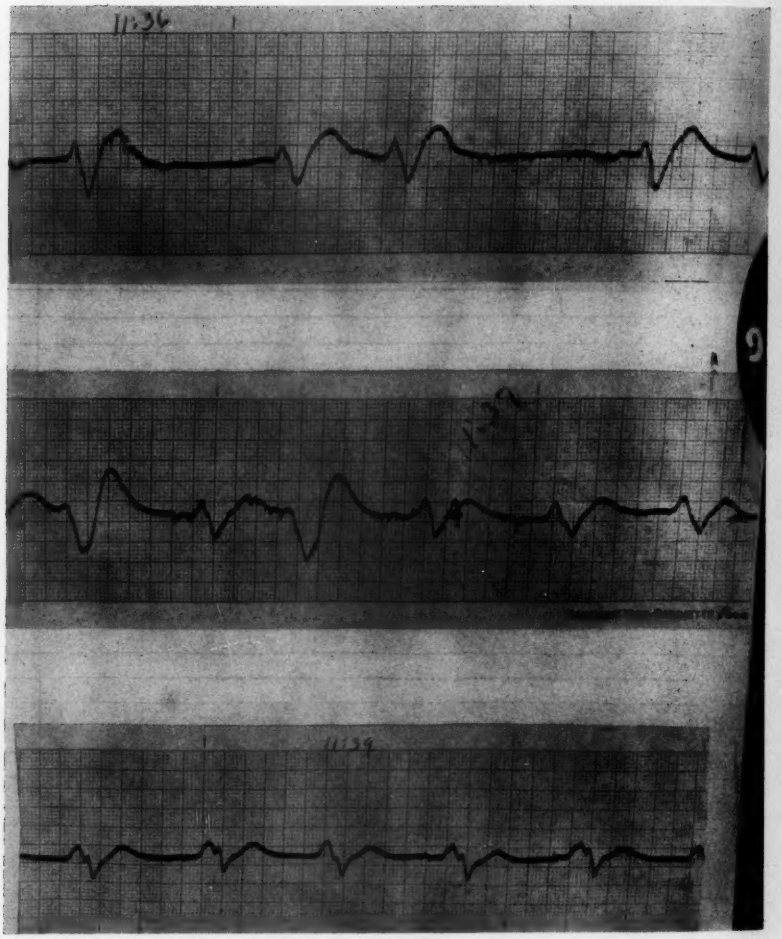

FIG. 10. First signs of rhythmic beats after cardiac standstill

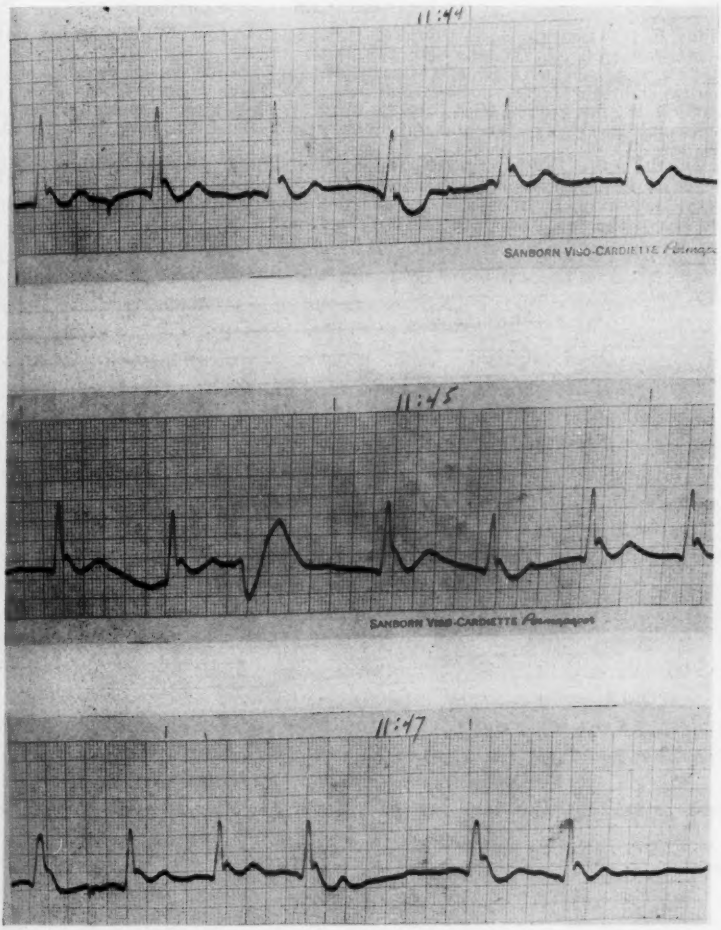

FIG. 11. Improvement in rhythmaticy after cardiac standstill

22, 1955. He has been working full time since May 18, 1955. His electrocardiograms have continued normal. The last basal metabolic rate was minus 19.

The pathologic report was that of "diffuse toxic goiter with moderate involution."

CONCLUSION

It is our conclusion that surgery could not have been carried out in this patient without hypothermia. While his convalescence and hospitalization were prolonged by the thoracotomy and burns, even this was much less than a more conservative regime would have allowed, and, while it is pure speculation, I doubt that he would have reached a euthyroid state.

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CLINICAL HYPOTHERMIA: A STUDY OF THE ICEWATER SURFACE IMMERSION AND SHORT-WAVE DIATHERMY REWARMING TECHNICS*

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Several methods have been advocated for subjecting patients to varying levels of hypothermia for surgical or other therapeutic purposes. The earlier workers, using only mild sedation or light anesthesia, placed the unclothed patient in a room in which cool air was circulated.[19, 25, 26] Delorme,[9] Ross[22] and Juvenelle,[17] recommended extracorporeal cooling of blood for rapid induction of hypothermia under deep anesthesia. Blades, et al[5], poured cold saline solution into the open chest cavity. Others,[26, 8] have circulated cold water through coils in a blanket wrapped around the patient. For rewarming, the above methods were applied except that warm solutions were used in the place of the cold. In addition, Bigelow, et al,[3] also has recommended the use of high radio frequency for rewarming.

At the University of Colorado, ice water at a temperature of 0–5 C. has been used for cooling the patient by surface immersion and short-wave diathermy (occasionally supplemented by a warm water bath) has been used for rewarming. Cooling usually was accomplished more rapidly than rewarming by these means. During the process of cooling, a significant period of time elapsed before the sigmoid temperature began to drop, after which cooling proceeded more rapidly. Following removal of the patient from the tub there was a considerable *"after fall"* of body temperature. Upon institution of rewarming a longer lag period of time supervened before sigmoid temperature rose 1 C.

The present report is an evaluation of our technics used for cooling and rewarming.

METHOD

Studies were done in the operating room on patients undergoing intracardiac surgery with total circulatory occlusion. The patients received preanesthetic medication consisting of appropriate doses of demerol and scopolamine in a manner customary to preparation for any general anesthesia.[27] Induction was performed with pentothal or cyclopropane and anesthesia maintained with ether. The patient was hyperventilated by the anesthesiologist throughout the procedure in order to maintain a substantial respiratory alkalosis. d-Tubocurarine was administered prior to and during cooling whenever necessary to reduce shivering or muscular tightening. When the patient was in surgical

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TABLE 1

Time relationships during cooling and rewarming

	No.	Patient	Age	Body Surface Area (M^2)	Diagnosis*	Control Temp. (°C.)	Cooling							Rewarming		
							Removal from ice	Tub time	After fall	After fall time	Final temp	Total fall	Total time	Temp. diath. disc.	Deg. war.	Time
Group I. Children	1	P. S.	7	0.86	IASD	37.0	31.0	:23	5.0	:23	26.0	11.0	:46	34.0	8	1:10
	2	B. J.	4	0.50	IVSD	37.0	31.5	:27	3.5	:49	28.0	9.0	1:16	34.0	6	3:20
	3	H. B.	10	1.04	IASD	37.5	30.2	:70	3.2	:44	27.0	10.5	1:54	33.2	6.2	2:36
	4	S. S.	3	0.61	PVS	37.4	33.2	:18	4.2	:45	29.0	8.4	1:03	34.0	5	1:10
	5	L. B.	3	0.56	PVS	37.0	33.3	:14	2.1	:45	30.8	6.2	:59	34.0	3.2	:43
	6	H. T.	4	0.83	PVS	37.2	32.0	:49	5.2	:44	27.0	10.2	1:33	33.0	6	:58
	7	R. B.	6	0.75	TF	37.0	32.0	:20	4.0	1:20	28.0	9.0	1:40	34.0	6	1:30
	8	E. C.	8	0.82	TF	37.5	33.0	:20	5.0	1:26	28.0	9.5	1:46	33.0	5	1:45
Group II. Adults	1	E. A.	27	1.36	IASD, PDA	37.0	31.5	:53	5.5	:53	26.0	11.0	1:46	33.5	7.5	3:31
	2	T. G.	32	1.45	IASD	37.0	31.0	:42	5.0	1:06	26.0	11.0	1:48	34.5	8.5	2:30
	3	F. H.	31	1.54	IASD	37.2	31.0	:52	5.0	:40	26.0	11.2	1:32	33.5	7.5	2:56
	4	H. H.	35	1.67	IASD, IVSD	37.0	31.0	:50	4.7	:55	26.3	10.7	1:45	34.0	7.7	3:25
	5	J. St. J.	20	1.76	IASD	37.0	31.0	1:07	3.0	:50	28.0	9.0	1:57	34.0	6	2:28
	6	R. M.	14	1.32	PVS, PDA	37.0	32.6	:52	3.6	:36	29.0	8.0	1:28	34.0	5	1:52
	7	S. P.	17	1.50	PVS	37.0	33.0	:35	4.2	1:20	28.8	8.2	1:55	31.0	2.2	1:57

* IASD—Interatrial Septal Defect; IVSD—Interventricular Septal Defect; TF—Tetralogy of Fallot; PDA—Patent Ductus Arteriosus; PVS—Pulmonary Valvular Stenosis.

anesthesia (second plane, third stage), he was placed in a tub of water having a temperature of 15–18 C., and observed for a few minutes. The electrocardiograph was continuously monitored by a cathode ray oscilloscope. Upon assurance of adequate control of muscle activity and no undue disturbance in electrocardiogram, ice was added, reducing the water temperature to 0–5 C. As cold narcosis set in, the amount of ether administered was reduced. Again muscle relaxants were given as needed. Generally, when the body temperature began to fall, little additional paralytic agent was required. The temperature was recorded by a thermocouple inserted into the rectosigmoid. Some difference of opinion exists as to reliability of the sigmoid temperature as an index of the body temperature. However, substantial evidence has been presented that sigmoid temperatures are within 1 degree centigrade of that found in other internal organs.[1] For clinical purposes it was our belief that this degree of accuracy was quite adequate.

When the desired level of sigmoid temperature was reached, the patient was removed from the ice bath and placed on the operating table. The skin was carefully dried, particularly the trunk, pelvis and perineum. The lower trunk and pelvis were encased in protective padding around which were draped diathermy coils. (Thus rewarming could be instituted at an instant's notice). Eventually, administration of the anesthetic agent was terminated and the patient was respired with oxygen only. At varying temperature levels, the blood pressure was lost to auscultation and often the pulse to palpation. Direct intra-arterial pressures were monitored through a carrier-type amplifier on a cathode-ray oscilloscope.

Upon conclusion of the actual intracardiac operative procedure, rewarming was started with diathermy (2 minutes on and 1 minute off). This intermittent application was elected to avoid skin burns. Usually as the temperature rose, no additional anesthetic agent was required. In some, however, supplemental nitrous oxide-oxygen was needed. When the sigmoid temperature reached 34 C. active rewarming was terminated and the patient was removed to the recovery room. Normal body temperature was achieved spontaneously within 4 to 8 hours.

OBSERVATIONS

Fifteen patients with congenital heart disease, cooled to a range of 26 to 31 degrees centigrade, were studied. Data relative to age, cardiac defect, body surface area* and times of cooling and rewarming appear in table I. For purposes of evaluation of data, the patients were divided into two groups based on age. Group I consisted of patients less than 11 years old.

Cardiovascular Phenomena

The anesthetized patient upon immersion in the bath tub often exhibited some tightening of muscles or even actual movement, particularly after the ice

* Dubois Formula:

$$\text{BSA } (m^2) = \text{Wt. (Kg.)}^{.425} \times \text{Ht. (cm.)}^{.725} \times 71.84$$

was added. This generally was allayed with d-tubocurarine. The skin, in a few minutes, turned bright pink. This was sharply demarcated and limited to those regions of the body in direct contact with the ice water. Details of cardiovascular changes are described elsewhere[6]. Briefly, the following events were observed: The blood pressure underwent a transient elevation and then entered a gradual decline. The heart rate did not accelerate, but progressively slowed as the patient cooled. Shortly afterward, the blood pressure by auscultation could not be obtained. Direct arterial pressure tracings showed that, despite the clinical "*loss*" of the pressure, it was still quite adequate. Later as the temperature dropped further, the pulse could no longer be felt. Direct measurements again proved that the blood pressure and pulse pressure were quite definite. When a predetermined arbitrary temperature level was reached, the patient was removed to the operating table. A further drop in body temperature ensued. Finally, about 30 minutes after the low temperature was reached, the blood pressure stabilized at its lowest level. The heart rate, which already had reached its lowest level at the same time as the temperature, exhibited no further drop. The pink color faded and the skin became quite pale. Following the surgical procedure, rewarming was begun. The blood pressure slowly began to increase and the heart to accelerate. The blood pressure became auscultatable and the pulse palpable. Both began to approach normal and at 34 C., the point at which diathermy was stopped, they were within normal limits. The patient was extubated, began to move and responded to vocal stimuli. The skin was pale.

Hypothermic Anesthesia

At varying temperature levels, the subjects entered hypothermic anesthesia (narcosis due entirely to cold). The administration of ether was terminated and the patients were given oxygen only. Data relative to duration of administration of the anesthetic agent and temperatures at which cold narcosis was presumably attained are grouped in table II. It will be noted that there was considerable variation in temperature levels at which cold narcosis was reached, ranging from 34 to 27 C. The majority of the patients, however, entered hypothermic anesthesia at 31 C. or below, which was at about the time the patients were removed from the tub. The exact time could not be precisely determined since varying levels of analgesia to cold existed, and since the amount of residual ether analgesia could not be assessed. At the time of the thoracic incision, however, the patients were essentially under hypothermic anesthesia alone, the ether having largely been exhaled.

The pupils of the patients at this time were fixed in the midline but usually were quite large, evidently due to the lack of any pharmacologic anesthetic agent. In a few patients who were especially sensitive to opiate, the pupils remained small. Superficial reflexes were absent. A few patients needed to have additional d-tubocurarine after removal to the operating table, to prevent various movements, or to relieve a muscular tonus strong enough to prevent proper positioning of arms and legs. None of the patients required any agent for analgesia or for hypnosis.

TABLE 2

Hypothermic anaesthesia

		Temp. when Ether Stopped	Total Ether Time	Temp. of Cold Narcosis	Time of Cold Narcosis	Supplemental Anaesthesia During Rewarming			Total Anaes. Time
						Agent	Temp. begun	Dur. rewar.	
Group I	P. S.	32.5	1:00	32.0	2:30	N_2O–O_2	30.0	:30	4:00
	B. J.	31.5	1:50	29.0	3:05	N_2O–O_2	30.8	:30	5:25
	R. B.	30.2	1:15	30.0	3:45	N_2O–O_2	30.0	:20	5:10
	S. S.	33.4	1:10	34.0	3:30	None		—	4:40
	L. B.	31.0	1:15	31.0	2:15	N_2O–O_2 Cyclopropane	32.6	1:10	4:40
	E. C.	31.0	1:55	31.0	2:45	N_2O–O_2	30.8	:30	4:10
	H. T.	31.0	1:30	31.0	2:45	N_2O–O_2	33.2	:15	4:30
	H. B.	31.0	1:50	31.0	3:35	N_2O–O_2	30.6	:25	5:50
Group II	E. A.	32.5	1:20	32.0	4:00	None		—	5:20
	T. G.	29.0	1:00	29.0	3:30	N_2O–O_2	30.0	:30	5:00
	F. H.	27.0	1:20	27.0	3:35	None		—	4:55
	H. H.	32.0	1:50	28.0	1:35	N_2O–O_2	26.7	:25	4:55
	J. St. J.	31.0	1:55	31.0	3:05	None		—	5:00
	R. M.	33.0	1:35	33.0	3:40	None		—	5:15
	S. P.	29.0	2:00	29.0	3:20	None		—	5:20

During rewarming, 9 of the 15 patients required supplemental nitrous oxide-oxygen because of return of muscular movement. This was started at varying temperature levels, usually at about 30 C., and continued until the operative procedure had been completed.

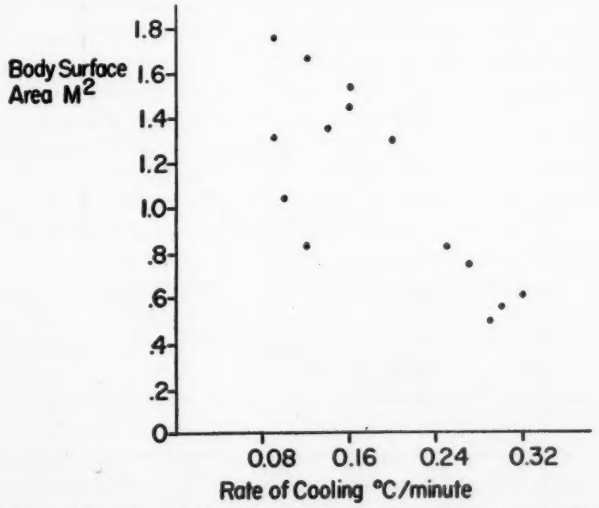

FIG. 1. Relation of body surface area to rate of cooling. There is a direct relationship between body surface area and rate of cooling.

Rates of Cooling and of Rewarming

The times of (1) cooling in the ice bath, (2) further temperature drop out of bath, (3) total to stabilization at lowest temperature, and (4) rewarming may be noted in table I. The nature of the congenital heart lesion had no apparent relation to the rate of cooling or warming. The only positive correlation to rate of cooling appeared to be the body surface area of the patient (fig. 1).

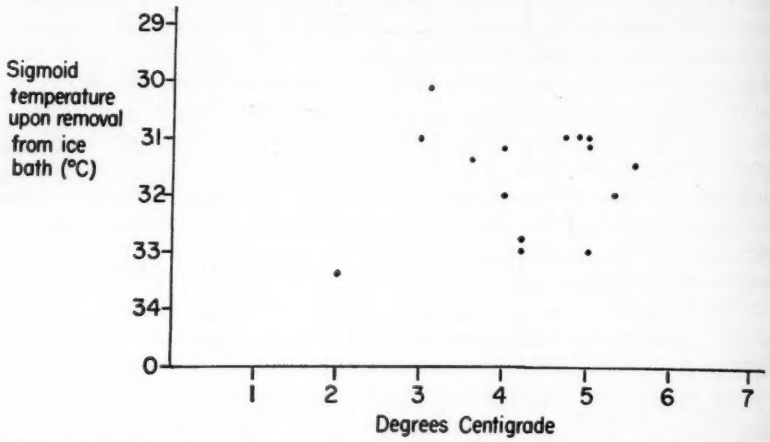

FIG. 2. Relation between end tub temperature and "after fall." There is no apparent relationship between temperature at time of removal from tub and the "after fall."

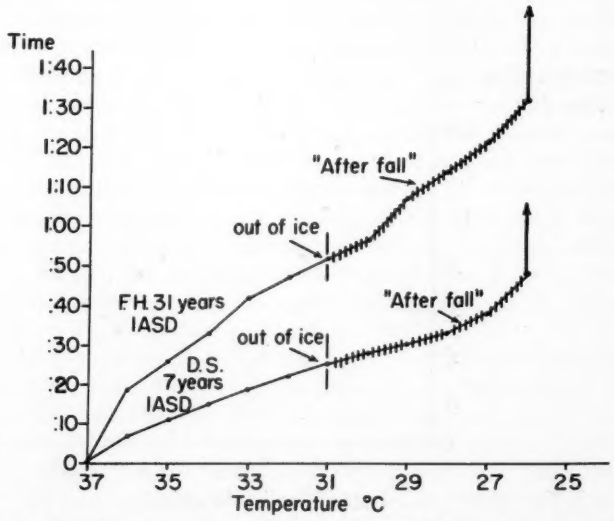

FIG. 3. Rates of cooling in ice water bath and "after fall." After overcoming the temperature "barrier", the rate of fall of sigmoid temperature accelerates. In the child it approaches linearity with time.

One of the most important problems in clinical hypothermia is the decision as to when the patient should be removed from the ice bath in order to achieve a predicted further fall in temperature. This fall in our group of patients varied from 2.0 to 5.5 C. The sigmoid temperatures at which the patients were removed from the ice bath ranged from 33 to 30.2 C., with the majority falling between 31 and 32 C. The period of anticipated total circulatory occlusion influenced the decision regarding the desirable end temperature and thus also the temperature at which the patient was to be removed from the bath. Figure 2 shows the relationship between temperature at which the patient was removed and the *"after-fall"*. There was no linear relationship between the two variables.

A significant period of time elapsed between the exposure of the patient to the water and the change in rectal temperature. In Group I, the average time for the rectal temperature to drop 1.0 C. was 6.5 minutes. In Group II, the adults, the time interval was 14.9 minutes. A similar lag was observed during rewarming. The general statement may be made that a longer period of time elapsed for the sigmoid temperature to rise 1 C. on rewarming by diathermy than to fall 1 C. upon institution of cooling by tub immersion.

DISCUSSION

Most previous observations concerning the reaction of human beings to cold were made in an ambient air environment.[7, 11, 23] On the basis of these studies, the initial response of the unanesthetized person upon exposure to cold air (usually at about 18 C.) is believed to be mediated through vasomotor control. This consists of mass peripheral vasoconstriction with vasodilatation in the muscles, in the splanchnic region,[4, 20] and possibly in the lungs.[12] The net result of this response is diminished rate of loss of body heat.[7] This is accomplished by two means:[18] (1) diminished fluid transport to the body surface, and (2) increase in the insulating properties of the cutaneous and subcutaneous tissue layers. Heat loss occurs through the physical conduits of radiation, convection and evaporation, but not conduction, with a significant increase in convection and decrease in evaporation upon exposure to cold air.

It generally is agreed by those who studied such conscious patients that the rate of heat loss is directly proportional to the body surface area,[11, 28, 21] and inversely proportional to the body specific gravity.[21]

Heat is lost from the body in the ice water surface immersion technic of cooling predominantly through conduction.[10] However, in our experience, convection also proves to be an important factor. Heat transferred from the body to the immediately adjacent ice water produces a zone of water around the body considerably warmer than the rest of the tub, thus reducing the speed of cooling. To insure maintenance of constant body contact with 0–5 C. water, persistent agitation of the water is necessary. Other factors affecting rate of cooling are (1) composition of the body and (2) body surface area. Individuals with abundant subcutaneous fat have a thicker insulating surface layer than lean individuals. The size of the individual, irrespective of body composition, however, proves to be the constant factor in temperature regulation. A direct relationship was found in this study between body surface area and the speed of cooling.

It has been demonstrated that the unanesthetized subject, exposed to a cold environment, exhibits marked shivering.[7, 11, 23] This is a favorable reflex mechanism which promotes heat production and succeeds in maintaining a normal body temperature in the face of marked reduction in skin surface temperature. However, when the lowering of body temperature is the goal, shivering not only stalls the procedure but possibly may contribute to the development of cardiac arrhythmias. In addition to promoting the comfort of the patient, the objective of adequate anesthesia, then, is to control shivering, permitting a safe, rapid fall in body temperature to the desired level without undue depression of circulation. Maintenance of an adequate circulation during anesthesia is of prime importance to the speed of cooling, especially the distribution of that circulation to the periphery.

We believe the following is the course of vascular events which occur under the conditions of our study. When exposed to the ice water, an intense peripheral vasoconstriction develops, which is both direct and reflex in origin. After a time this is followed by peripheral vasodilatation, due to the direct effect of cold. Following this, the circulating blood cools and the larger vessels begin to constrict, again due to direct cold effect. Following removal from the ice water and the gradual disappearance of internal gradients, peripheral vasoconstriction again occurs.

The interesting delay before the body temperature begins to fall, we describe as a *"temperature barrier"*. The principal ramparts of this *"barrier"* consist of (1) diminished peripheral blood flow, and (2) increase in tissue insulating depth. These two factors result from the intense vasoconstriction peripherally, which is in part direct and in part reflex.[13] The increased tissue insulation impedes the conduction of that heat which is brought near the surface by the markedly diminished blood flow. In this way, body heat is protected and confined to the deeper parts and the body temperature is normal despite a pronounced cooling of the skin. The peripheral vasoconstrictor toe-hold is lost as cold paralysis grips the peripheral vessels and vasodilatation develops. The sharp demarcation of the pink skin at the water-line is a very striking and uniform observation. The blood flow to the surface now is increased, body heat is lost rapidly and the temperature begins to fall. The *"temperature barrier"* has been overcome. From this point on, vasomotor responses no longer regulate cooling, which becomes a function of mass and time, provided the total circulation is adequate. As the temperature of the blood cools, the larger vessels constrict, due to the direct effect of the cold blood.[2, 24] This is manifested by clinical *"loss"* of blood pressure, while the pulse itself usually *"disappears"* as the vascular system becomes relatively rigid.

Greenfield,[14, 15] noticed a similar lag in vasodilatation in studies on the immersion of human hands and feet in cold water.

When the patient is removed from the ice bath, the sigmoid temperature continues to fall. Similar observations were made in the notorious Dachau studies.[16] This *"after-fall"* is due to large temperature gradients between the skin surface, parietal structures and the internal organs. Temperature measure-

ments of muscle just beneath the skin have demonstrated wide gradients upon removal from the ice bath. In one patient (K.P.), the muscle temperature was 6 C. and the sigmoid 33 C., giving a gradient of 27 C.

A redistribution of heat within the body now occurs by means of the circulation. The gradients gradually decrease, the rate of fall in sigmoid temperature declines, and finally halts as all tissues achieve a fairly uniform temperature level. The patient then is in a state of stable hypothermia. The paralysis of the peripheral vessels is relieved as the skin warms, peripheral vasoconstriction again occurs and the skin becomes uniformly pale.

The rate of rewarming will depend on the adequacy of the circulation and the effectiveness of the method of heat supply. The heart itself is of prime concern. Following circulatory occlusion with diminution of coronary blood flow, and as a result of operative manipulation, the resumption of adequate myocardial function may be delayed. Occasionally, of course, a major disturbance in rhythm, such as ventricular fibrillation, may occur, and its treatment will further delay the return of myocardial function (patient no. 2 in table I is an example). The underlying pathology and the state of the myocardium at the time of surgery is believed to be an additional factor. The dilated failing heart of the advanced stages of atrial septal defect is less capable of resuming function than the simple hypertrophy of pulmonary stenosis. Moreover, the circulation may be jeopardized by a low blood volume if operative blood loss has been extensive, yet rate of transfusion must not exceed the capacity of the myocardium, thus causing further delay. The method used to return the patient toward his normal body temperature also modifies the speed of rewarming. Short-wave diathermy, in contrast to surface immersion, warms the deeper parts of the body. Intermittent interruption of efficiency of heat production in the patient may occur because of electromagnetic field interference by the operating table, instruments or adjacent wires, or close contact by members of the operating team. Moreover, only a portion of the body is subjected to the electromagnetic field. Subject to these factors, the speed of rewarming, as with cooling, is primarilya function of body mass.

The considerations above should be recognized as holding an important corollary regarding any evaluation of cooling and warming methods; namely, that there are significant physiologic differences during cooling and rewarming between the patient undergoing surface immersion and the patient undergoing perfusion or diathermy. The specific temperature effects on the peripheral vessels are not present in the latter technics, and the central-peripheral temperature gradient is absent, or even reversed. In addition, with perfusion, the heart and lungs are primarily and differentially affected in relation to other organs or the parietes. The importance of these differences is not fully understood, but we emphasize that surface and internal cooling and warming methods differ in much more basic aspects than convenience, speed or aesthetics. On the other hand, once the stable hypothermic stable has been achieved, these differences have largely disappeared, and the physiologic situation probably is the same.

SUMMARY AND CONCLUSIONS

1. Study has been made of the surface immersion cooling and short-wave diathermy rewarming of human subjects.

2. The rate of cooling was variable and was primarily a function of body size and shape (surface area). During surface immersion cooling, temperature exchange is accomplished largely by conduction, but convection by agitation of the ice water is important.

3. Upon exposure to ice water (0–5 C.) an initial delay in the fall of 1 C. in sigmoid temperature was noted. This lag is due to a "*temperature barrier*", consisting of a diminished peripheral blood flow. The subsequent development of peripheral vasodilatation, due to the direct effect of cold, allows cooling to proceed as a function of time and mass.

4. An "*after-fall*" in the sigmoid temperature of 2 to 5½ degrees centigrade occurred upon removal from the ice bath. This is due to the redistribution of heat within the body as internal temperature gradients are lessened by the circulation. "*After-fall*" could not be predicted with precision, and was not related to any identifiable variable.

5. Rewarming by short-wave diathermy was effective. It is not a surface technic and is not associated with large internal gradients or specific peripheral circulatory changes.

6. Hypothermic anesthesia developed at varying temperature levels, usually below 31 C. sigmoid temperature, thereby permitting the cessation of other anesthetic agents. Hypothermic anesthesia was adequate for open chest procedures and lasted throughout most of the period of rewarming. In 9 of 15 patients, supplementary nitrous oxide was required for the final stages of the procedure.

7. Different physiologic states exist during cooling and rewarming when surface and perfusion technics are used, although during the stable state of hypothermia the physiologic situation probably is the same with both methods.

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PHARYNGO-ESOPHAGEAL DIVERTICULA

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A diverticulum may occur at any portion of the esophagus; it is found most frequently in the pharyngo-esophageal area, and less frequently in the mid-thoracic esophageal and epiphrenic areas.

The pharyngo-esophageal type of diverticulum usually is a so-called pulsion type, in that it apparently is formed by pressure from within out and essentially consists of herniated mucous membrane with only vestiges of attached esophageal muscle. It can perhaps be compared to the sac of an inguinal hernia of the acquired type. One of the etiologic factors that may be of significance is a presumed weakness at the junction of the pharynx and esophagus. This presumed weak area lies just superior to the cricopharyngeus muscle and is an area where pharyngeal constrictors and cricopharyngeal muscles meet. Apparently age also is of significance, as most patients with esophageal diverticula are in the older age groups. Spasm, stricture, hiatus hernia, esophagitis, or any obstruction of the esophagus may increase intraluminal pressure, and thereby contribute to development of esophageal diverticula.

DIAGNOSIS

It is quite simple to diagnose esophageal diverticula if one is thorough and investigates each patient who complains of symptoms referable to the esophagus.

The patient may have various symptoms, but in those patients who have diverticula located at the pharyngo-esophageal area, the most common complaint is dysphagia, varying from a slight degree to complete obstruction. Those with obstruction have weight loss, dehydration, and occasionally vitamin deficiency. Regurgitation of food and fluids is another frequent complaint, and some patients fear sleeping, as they awaken because of choking on aspirated food, or the pillow is wet and soiled with regurgitated fluid the next morning. Occasionally aspiration of regurgitated food will lead to pneumonia, lung abscess, or chronic pulmonary disease (fig. 1). Other complaints may be halitosis, a gurgling noise in the neck, a sensation of fullness in the neck, and occasional nausea.

Physical examination usually reveals little unless obstruction has caused weight loss and malnutrition. A large diverticulum sometimes may be demonstrated as a soft cervical mass, made evident by the Valsalva maneuver. One sign[3] often positive, consists of a gurgling noise in the neck after the patient has drunk water and the examiner palpates the thyroid area.

Roentgen findings vary from a small dimple to sacs as large as a grapefruit (figs. 2, 3). With the larger diverticulum, there usually is some degree of obstruction which is obvious on roentgenologic study. The sac of a diverticulum also may vary in shape, and may present to the right, left, or midline.

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FIG. 1. Aspiration pneumonitis secondary to an esophageal diverticulum

FIG. 2.

FIG. 3.

FIG. 2. A double pharyngo-esophageal diverticulum

FIG. 3. A very large pharyngo-esophageal diverticulum extending down the mediastinum to the level of the aortic arch.

Esophagoscopy and dilatation are not essential to diagnosis, but should be carried out if there is any question as to the presence of malignancy or distal esophageal obstruction.

TREATMENT

The historic aspects of the surgical treatment of esophageal diverticula are well documented, and have been thoroughly reviewed by Lahey and Warren[6] and by DeBakey, Heaney, and Creech.[4]

As some of the older methods are occasionally *"revived"*, it might be well to review the cause for failure in early methods. The suggestion by Bell[1], in 1830, that such diverticula might be treated by converting the diverticulum into an external fistula was practiced by Nicaladoni[9] in 1877. The disadvantages of such a method are obvious, as most of the food swallowed goes out the fistula. Nicaladoni's patient died of pneumonia a few days after surgery. An external esophageal fistula of large size is not compatible with life, as it imposes severe problems of nutrition and infection.

Niehans,[10] in 1844, did the first one stage diverticulectomy, and it probably would have been successful except for trauma to the superior thyroid artery with hemorrhage and death a few days postoperatively.

Invagination of the sac was proposed by Girard[5] in 1896, and Bevan[2] revived this method. The disadvantage of this method is that the sac usually is thin and will not satisfactorily hold adequate inversion sutures, and recurrence takes place. Cases also have been reported in which the inverted sac has been regurgitated with resultant laryngeal obstruction.

Mosher[8] attempted endoscopically to open the wall between the esophagus and the sac of the diverticulum, which was a diverticuloesophageal anastomosis of sorts. This procedure was attended by a prohibitive mortality rate due to infection and mediastinitis.

Diverticulopexy, or the first stage of a two stage resection has had its advocates, but the recurrence rate is high, in that the sac tends to sag and soon is again dependent.

In all but exceptional cases, the two stage, or one stage diverticulectomy is now the accepted treatment.

For many years, Lahey[6] championed the two stage operation, stating that the mortality rate was low. In his series of 365 cases, there were only 2 deaths, the recurrence rate was only 4.8 per cent, and morbidity rate also was low. In his early experience, the hospital time required for this method averaged 19 to 21 days; in the later experience, the total hospital time averaged 14 days.

Advocates[7] of the one stage diverticulectomy procedure point to a comparable mortality and morbidity rates, and a shorter period of hospitalization. Of course, the desirability of only one operation and one anesthetic is obvious from the standpoint of patient appeal and economics.

The Baptist Memorial Hospital has had 17 patients who were operated upon for pharyngo-esophageal diverticula by various members of the resident and attendant staffs. Seven of this number had a two stage resection, 7 a one stage

resection, and 3 patients have had only the first stage of a two stage operation. There have been no deaths among this group, and all were relieved of their complaints.

Postoperative complications occurred in 6 patients. There was a pharyngo-salivary-cutaneous fistula in 1, electrolyte deficiency in another, shock in 1, stricture in 1, and temporary dysphagia in 1. All of these complications were relieved without difficulty.

TECHNIC

As the preferred method of the author is the one stage diverticulectomy, remarks regarding technic will be confined to this method.

Little is required preoperatively except the sac must be empty, and if malnutrition is severe, this should be corrected, if possible. The former can be accomplished by passage of a Levine tube the morning of surgery. It usually passes right into the sac, and a small amount of fluid can be aspirated. It is not necessary to leave the tube in place. Methods of relieving malnutrition are well known to all. It is thought that gastrostomy is rarely, if ever, indicated as a preoperative measure.

General anesthesia, with an endotracheal tube and gauze packing off of the larynx is preferred. Block anesthesia, however, is satisfactory. Proponents of the block method maintain it is more satisfactory in that it prevents aspiration of fluid during surgery. Patients are sometimes uncomfortable, however, when they must lie still for an hour, which is the average operating time, and some find it difficult to refrain from swallowing if they are awake. Of course, this causes movement of the surgical field.

The roentgenogram reveals the side where the diverticulum presents, and incision should be made on that side. Incision along the anterior border of the sternomastoid muscle is preferred, but a collar type of incision is satisfactory and perhaps is more cosmetic.

One enters the fascial space just anterior to the sternomastoid muscle. The carotid artery, jugular vein, and vagus nerve are retracted laterally, and the thyroid gland and trachea retracted medially. The prevertebral space then is identified; the sac lies immediately anterior to this space at the level of the cricoid or below.

The sac then must be dissected free with all muscle fibers dissected back, particularly at the neck of the sac (fig. 4). One should avoid tenting the esophagus with excessive traction, and by the same token, avoid under dissection, and thereby leave a portion of sac unremoved. Following dissection of the neck of the sac, a clamp is placed across it, and by the cut and sew technic, one removes the sac and closes the defect bit by bit (fig. 5). This leaves no traumatized or crushed and necrotic tissue, a very important consideration to wound healing in an area of poor blood supply and no serosa. The knots are placed so they are intraluminal and 3 no. 0 silk sutures are used. A second row of sutures then approximates the muscle fibers, a Penrose drain is inserted, and the wound then closed in layers.

FIG. 4. The diverticulum is mobilized and all muscle fibers are dissected back from the neck of the sac.

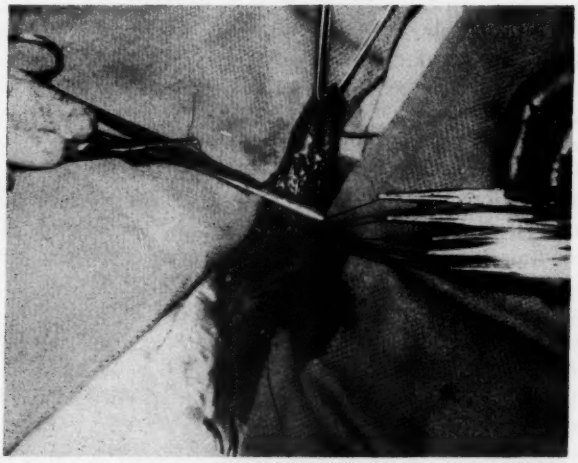

FIG. 5. Following isolation of the neck of the sac, a clamp is applied and by cut and sew technic the sac is removed and esophagus closed. In this view the sac is half cut across and five sutures have been placed and tied.

Postoperative care consists of restriction of oral feeding for about 2–3 days. The drain is removed on the fifth postoperative day, and the patient is dismissed from the hospital on the sixth or seventh day. Prophylactic antibiotics are used routinely.

SUMMARY

Although esophageal diverticula are rare, it is mainly a disease of the older population, and as such will be seen with increasing frequency in years to come.

Diagnosis is easy if one is thorough and roentgenograms will be positive in nearly every case.

When symptoms are due to the presence of a diverticulum, resection is indicated—the one stage method is preferable.

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BASAL CELL CARCINOMA OF THE ANUS

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Basal cell carcinoma of the anus has been diagnosed and reported only 31 times since Pennington[16] described the lesion for the first time in 1923. Buie and Brust[5] found only 2 cases out of 2,939 malignant anorectal tumors studied by them in 1933. Guess[8], in 1935, stated that he found no tumor of this type listed in the records of 150,000 biopsies done at the State Institute for Malignant Disease at Buffalo.

Because the development of basal cell carcinoma is so rare in the anal region, an additional case is reported here.

Ackerman and del Regato[1] state that when this tumor involves areas of unexposed skin it tends to be multiple. The patient described had 4 basal cell tumors on her back in addition to the 1 in the anus. Histologically they were identical.

CASE REPORT

Case History: G. H., a 66 year old white woman, was first seen in the Tumor Clinic on Nov. 16, 1954 complaining of sores on the upper and lower back, as well as about the anus. She stated that they had been there for about 4 to 5 years, and would not heal despite the application of ointments and creams. The lesions which began as small spots began to grow, and she thought they were now about the size of a *"half dollar"*. During this time, she had noticed itching, burning, draining of clear liquid, and occasionally blood. Her appetite had been good, with no weight loss; her bowel movements had been regular. There was no melena. In 1952 a tumor was removed from the right shoulder, the pathology of which was basal cell carcinoma.

Physical Examination: The patient was a well developed, well nourished, white woman in no acute distress. There was a fine tremor of all extremities. The back showed a healed scar on the right superior shoulder. In the dorsal midback, in the region of the seventh thoracic vertebra, there was a crusted raised lesion, 3 mm. in height, with pearly edges 4.5 cm. in diameter, nontender, and not attached to the underlying fascia. In the lumbar midback, in the region of the second lumbar vertebra, there was another crusted lesion, 5 cm. in diameter, nontender and pearly edged. Rectal examination showed a lesion on the right lateral border of the anal orifice 2.5 by 3 by .5 cm. extending from the mucocutaneous junction (fig. 1). The sphincter tone was good and there were no masses palpable in the rectum. Proctoscopic examination failed to show any extension into the rectum. Lymph node examination failed to show any adenopathy.

Biopsy of the three lesions showed basal cell carcinoma of all three. The patient was admitted to St. John's Hospital on Dec. 12, 1954. Complete blood count, urinalysis, serology, chest roentgenogram, and electrocardiograph were all essentially within normal limits. Surgical removal of all lesions was advised.

Surgery: The lesions on the thoracic and lumbar back were excised with a border of normal skin 1.5 cm. in width. Pedicle flaps were swung into the excised area directly over the vertebral spine. The donor sites were covered with split thickness skin grafts. With the use of an electric cautery knife, an incision was made circumscribing the anal lesion with a 1 cm. border. This incision extended internally to the mucocutaneous junction. A portion of the external sphincter was excised. The rectal mucosa then was dissected free for a dis-

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FIG. 1. Basal cell carcinoma extending outward from anal canal

tance proximally of 1 cm., and this was then sutured to the remaining portion of the external sphincter fibers.

Pathologist's Report: (Dr. Emil Palik) "Specimen from the anus and adjacent skin consists of an irregular piece of white skin and subcutaneous tissue measuring 4 by 2.5 by 1.5 cm. Eccentrically placed, there is an irregular excrescence 3 cm. in height. Specimen from lumbar area consists of an ovoid piece of white skin and subcutaneous tissue measuring 4.5 by 4 by 1.5 cm. Specimen from the dorsal back consists of an elliptical piece of white skin and subcutaneous tissue measuring 6.5 by 4 by 1.6 cm. on the center of which there is an excrescence 4.7 by 1.8 cm. in size.

Microscopic Examination: Histologic examination of specimen from the anus shows a

FIG. 2. (30 ×). Basal cell carcinomatous invasion of the perianal structures. Note the presence of scattered apocrine glands in center of section, and sphincter muscle fibers in lower left.

TABLE I

(*After Martineau, and associates*[14])

This table includes all acceptable case reports to October 1955.

Author	Age	Sex	Duration of Symptoms Before Admission	Clinical Findings	Histopathology	Treatment
1. Pennington[16], 1923	53	M	About 6 years	Pruritus, hemorrhoids and fissures. Small granular nodules.	Basal cell carcinoma	Radium therapy
2. Wallon[21], 1927	63	M	About 4 years	Thick, friable, easily bleeding vegetations associated with hemorrhoids.	Basal cell epithelioma	Colostomy, radium therapy, followed by closure of colostomy.
3. Rosser[17], 1931	77	F	30 years	Hemorrhoids, blood stained pus from anus. Indurated anal tumor. Inguinal glands involved.	Epithelioma, presumably basal cell.	Not reported.
4. Buie and Brust[5], 1933	53	F	1 year	Advanced annular lesion.	Basal cell epithelioma	Colostomy; posterior resection, half of vagina removed. Local nodes removed, Radium.
5. Buie and Brust[5], 1933	53	F	30 years	Hard node, size of orange, left groin extensive.	Basal cell epithelioma	Radium advised, went home without treatment.
6. Buie and Brust[5], 1933	77	M	6 months	Papillomatous mass 1 by 2 by 5 cm. involving anal margin.	Epithelioma "basal cell"	None
7. Guess[8], 1935	52	M	"Hemorrhoids" 27 years. "Tumor" 1 year	2 cm. diameter ulceration with a hypertrophied papilla, the size of a pea.	Basal cell carcinoma	Local excision. Radon seeds.
8. Tucker and Hellwig[19], 1938	43	M	2 years rectal bleeding. One week pain.	Infected anal ducts, Enlarged papillae, resembled a tumor. Plus int. and ext. hemorrhoids.	Basal cell carcinoma	Local excision, roentgen therapy and radium.

9. Lawrence[11], 1941	73	F	1 year. Growth in anus.	Advanced, hard annular, fungating mass.	Basal cell carcinoma	Colostomy and later posterior resection of anus and rectum.
10. Lawrence[11], 1941	68	M	11 months. Protruding mass.	Hard, annular, fungating tumor mass 6 cm. in greatest surface diameter. Involving prostate and membraneous urethra.	Basal cell carcinoma	Loop colostomy followed 8 days later by posterior resection of anus and rectum.
11. Gabriel[6], 1941	70	M	2 years	Oval flat ulcer the size of the thumbnail, right anterior anal quadrant.	Rodent ulcer	Local excision by cutting diathermy.
12. Gabriel[7], 1946	63	F	3 years	Small, flat, raised papule, bluish pink in colour about the size of a shilling.	Basal cell carcinoma	Local excision by cutting diathermy.
13. Roux-Berger and Ennuyer[18], 1948	?	?	?	?	Basal cell carcinoma	Roentgen therapy
14. Lott and Alexander[12], 1949	62	F	Not reported, complained of itching and irritation.	A small area of thickening, about 1 cm. in diameter, beneath the mucosa at 2 o'clock.	Basal cell carcinoma	Local excision. Fulguration. Local irradiation (x-ray)
15. Wakely and Childs[20], 1949	62	M	4 years	Irregular ulcer with hard edge.	Rodent ulcer	Local excision
16. Wakely and Childs[20], 1949	64	M	Pimple on anus for "some years"	Anal ulcer	Rodent ulcer	Local excision
17. Wakely and Childs[20], 1949	56	M	5 years. Anal lump.	Irregular ulcer at anal margin.	Rodent ulcer	Local excision
18. Wakely and Childs[20], 1949	69	M	5 years	Irregular anal ulcer with hard edge.	Rodent ulcer	Local excision
19. Bacon[3], 1949	60	M	Not reported. Anal bleeding.	Anal lump	Basal cell epithelioma	Abdomino-perineal resection.
20. Bacon[3], 1949	52	F	Not reported. Burning pain and itching.	Anal mass	Basal cell epithelioma	Roentgen therapy, inguinal dissection.
21. Bernstein[4], 1949	82	M	?	Painful raised area	Basal cell epithelioma	Local excision.

TABLE I (*Continued*)

Author	Age	Sex	Duration of Symptoms Before Admission	Clinical Findings	Histopathology	Treatment
22. McQuarrie and Buie[15], 1950	50	M	Protruding hemorrhoids, 8 years duration.	Small int. and ext. hemorrhoids and an area of dermatitis on the right wall of the anal canal with a small underlying indurated process.	Basal cell epithelioma	Wide, local excision, radium therapy.
23. McQuarrie and Buie[15], 1950	53	M	Anal trouble, 7 years duration.	Indurated ulcer 3 by 1.5 cm. at the posterior margin of the anus.	Basal cell epithelioma	Wide, local excision and radium therapy.
24. Hall[9], 1952	58	M	Not reported. Hemorrhoids and a "granuloma" to the left of the anal opening on admission.	A flat polyp of the skin 1 cm. in diameter, on section a well circumscribed, grey gelatinoid mass.	Basal cell carcinoma of the skin. (perianal) adenoid type	Local excision.
25. Martineau, Saini and Clermont[14], 1953	62	M	5 years hemorrhoids, 1 year prolapse mass.	A flat polyp of the mucosa of the right ant. quadrant of the anus, without ulceration.	Basal cell epithelioma	Local excision. X-ray irradiation to site.
26. Klippel and Tomlinson[10], 1953	65	M	3 years	Granulomatous tissue with central ulceration.	Basal cell carcinoma	X-ray; abdominoperineal resection.
27. Armitage and Smith[2], 1954	69	F	3 years	Growth involving whole anus.	Rodent ulcer	Radium needles 6500 r.
28. Armitage and Smith[2], 1954	60	F	Piles for 6 months	Ulcer at anal margin	Rodent ulcer	Radium needles 6000 r. Later excision.
29. Armitage and Smith[2], 1954	59	M	1 year. Sore place	Anal ulcer with hard margins.	Rodent ulcer	Local excision.
30. Armitage and Smith[2], 1954	64	M	?	Ulcer at anal margin	Rodent ulcer	Radium needles 6000 r. Excision.
31. Manheim and Alexander[13], 1955	72	M	Fistula-in-ano. 20 years.	Bluish swelling the size of a nickel with the external opening of a fistula in the center.	Basal cell carcinoma	Wide, local excision.
32. Matt and Dilger, 1955	57	F	5 years	Fusiform flat polypoid mass. Firm not ulcerated.	Basal cell carcinoma	Local excision by cutting diathermy.

FIG. 3. (250 ×). Demonstration of the characteristic plexiform structure of basal cell carcinoma

tumor which is situated within the superficial portions of the anal mucosa and submucosa and is composed of compact nests of neoplastic epithelial cells having small, oval, hyperchromatic nuclei with scanty, faintly acidophilic cytoplasms (figs. 2, 3). The nuclei at the periphery of the cell nests are disposed in a palisade fashion."

The specimens from the dorsal and lumbar back showed the same histologic picture. The final diagnosis was basal cell carcinoma of anus, lumbar and dorsal back.

DISCUSSION

Because basal cell carcinoma of the anus is such an uncommon lesion, only three attempts have been made to survey the literature.[2, 13, 14] A comparison of the cases reported in these surveys, with verification by studying the actual reports themselves, indicated that several cases, for one reason or another, had been omitted. One case reported by Gabriel should have been excluded because histologically it was a mixed basal cell-squamous cell carcinoma.

Certain characteristics of the disease are apparent. The lesion most frequently arises in elderly people. The ages range from 43 to 82 years with an average age of 62 years. The lesion, so characteristic of rodent ulcer, is present for a considerable time. Excluding the cases of Rosser and Buie and Brust, which had had a mass for 30 years, the average duration was 4 years. In the entire series there were 21 males, 10 females and 1 case in which there was no note of sex. This ratio is in substantial agreement with that reported by Armitage and Smith[2]. Contrary to their findings the presence of an ulcer (10 cases) ranked second to the complaint of a lump or mass (20 cases). Other symptoms were; bleeding, hemorrhoids, itching and, rarely, enlargement of inguinal lymph nodes. Pain is not a prominent symptom.

In three-fourths of the cases, new growth was not suspected prior to the his-

tologic examination. This is substantially larger than the findings of Tucker and Hellwig[19] who reported that one-third of their malignant lesions, encountered in a series of 951 proctologic cases, were clinically considered to be benign. This certainly should emphasize the admonition that all tissue removed by anorectal operation should be submitted to microscopic examination.

In general the lesion presents itself either as an area of induration without ulceration which may be flat, polypoid or papular; as an irregular small ulcer with a hard margin or finally as a hard annular lesion involving the entire circumference of the anus. The nature of the lesion indicates the type of therapy advisable. The latter type carcinoma unquestionably demands abdomino-perineal resection and close observation of the patient for inguinal node enlargement with subsequent nodal dissection should such appear. The nodular and ulcerative lesions respond equally well to local excision with, or without, subsequent irradiation of the tumor site. It is probable that wide local excision in itself is sufficient, avoiding the undesirable morbidity associated with irradiation applied to the anorectal region.

Only about half of the authors reported the outcome of treatment so that statistically the long-term results of surgical or x-ray therapy are presumptive. Nevertheless the prognosis appears to be good except in the case presenting an annular type of lesion.

SUMMARY

The literature on basal cell carcinoma is summarized. A total of only 31 cases have been reported.

An additional case of basal cell carcinoma is reported.

Of the three clinical types of lesion the prognosis is good except in the annular lesion.

ACKNOWLEDGMENT

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ADDENDUM

Case and Caldwell (Case, T. C., and Caldwell, G. E., Am. J. Surg., *91:* 842 (May 1956) reported an additional case of basal cell carcinoma of the anus after this article had been set in print. Their patient was a seventy-two year old white woman with complaint of severe defecatory pain for the previous two weeks. An area of induration 2 x 2 cm. was present 1 cm. above the pectinate line. She received 3,800 r. She subsequently developed extensive rectal slough which required colostomy and died six months after radiotherapy due to cardiovascular complications.

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THE RELATIONSHIP OF SYMPTOMS TO PROGNOSIS IN ADVANCED PROSTATIC CARCINOMA*

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One of the cardinal principles traditionally governing the sound clinical management of a patient with malignant disease is the early recognition of the lesion that results from prompt reporting of a patient's symptoms to his doctor and equally prompt institution of proper diagnostic and therapeutic procedures by his physician.

It, therefore, seemed of interest to study the pretreatment symptomatology in patients with advanced prostatic carcinoma in order to see if any relationship existed between symptoms and their pretreatment duration with post-treatment 5 year survivorship.

Thus, the clinical records of 88 patients with prostatic carcinoma too extensive for any reasonable chance of successful surgical extirpation by radical prostatectomy[6] were reviewed.

In most patients, the diagnosis was confirmed histologically by tissue removed by transurethral resection or perineal biopsy with a Silverman needle; in those instances without tissue diagnosis, there was no reasonable doubt about the presence of this disease because of the ultimate clinical course of the patients.

These patients comprised two separate clinically controlled groups as follows:

Group I represented 44 patients who satisfied the following clinical criteria:

1. The serum acid phosphatase level was 3.0 Gutman[3] units or less.

2. The upper urinary tracts showed no evidence of unilateral or bilateral hydronephrosis.

3. There were no demonstrable bone metastases.

This group had the most favorable prognosis of all among a larger over-all series of 220 patients whose cases have been previously reported, all with advanced prostatic carcinoma, too extensive for radical prostatectomy. In this group satisfying the above mentioned clinical criteria, 59.4 per cent survived 5 years provided they were treated by bilateral orchiectomy[4] and stilbestrol, 5 mg. daily, and provided that they survived unassociated[2] disease.

Group II represented 44 patients who satisfied only one clinical criterion—namely, that every patient had demonstrable bone or lymph node metastases. This group had a 5 year survivorship rate of 12.1 per cent when treated by bilateral orchiectomy and stilbestrol, usually 5 mg. daily, provided that they survived unassociated disease. It is obvious, therefore, that this group had a very poor prognosis in comparison with Group I patients.

The symptoms studied were listed as follows:

(a) Acute urinary retention,

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TABLE I

	Acute Urinary Retention	Dysuria	Back Pain	Hematuria	Weight Loss	Unassociated
Group I, 44 patients.....	18	31	3	6	4	2
Group II, 44 patients.....	14	25	16	5	13	2

(b) Symptoms such as dysuria, frequency, nocturia, and hesitancy, etc., and hitherto referred to as dysuria,

(c) Back pain,

(d) Gross hematuria,

(e) Loss of weight, and

(f.) Unassociated symptomatology—patients who were initially referred to the hospital because of some unassociated disease such as inguinal hernia or pernicious anemia and were found, on careful physical examination, to harbor prostatic carcinoma which was essentially clinically silent.

Table I shows the incidence of these individual symptoms in the two separate groups of patients. It is apparent from table I that there is no significant difference as far as the symptoms of acute urinary retention, dysuria, or gross hematuria are concerned since there was approximately the same incidence in both groups of patients.

However, there is a significant difference in two symptoms—namely, back pain and weight loss, both of which occurred much more frequently in the Group II patients with the poorer prognosis.

Thus, it is apparent that the presence of a history of pain in the back or weight loss is significant and suggests strongly the presence of bone or lymph node metastases.

An analysis of the commonest symptom, dysuria, is presented in table II in terms of pretreatment duration in the two respective groups of patients. It is at once obvious from table II that there is no significant difference in the duration of this symptom in the two groups.

One cannot, therefore, assume that patients in Group II were more negligent in reporting symptoms than patients in Group I. It would appear from this analysis that the duration of symptoms is essentially the same in these two groups and one cannot attribute the more advanced state of the disease present in the Group II patients to any unwarranted delay in the reporting of symptoms to the doctor. These findings are consistent with those of Nesbit and Plumb[5] who

TABLE II

Duration of symptom of dysuria

	0 to 2 years	2 to 4 years	Over 4 years	Duration Unstated
Group I patients.....	18	4	4	5
Group II patients.....	16	4	1	4

observed that the average duration of symptoms before diagnosis in patients without metastases was 33.6 months as compared to 25 months in patients with metastases. Thus it is obvious that in their large series the duration was not longer but even shorter in the series with metastases.

It is reasonable to consider that the biologic propensities for growth were different in the cancers of Group I as compared to those of Group II patients and that we were dealing with biologically less active cancers in Group I which, although symptoms had been present just as long, had not produced metastases, elevation in serum acid phosphatase level, or hydronephrosis and which still carried a 59 per cent chance of 5 year survival following orchiectomy and stilbestrol therapy.

Dunphy[1] has elaborated further on the subject of the significance of time in the treatment of cancer and emphasizes the extraordinary variations in growth potential of different cancers.

SUMMARY AND CONCLUSIONS

Two groups of patients having prostatic carcinoma too extensive to permit radical prostatectomy were studied with respect to symptoms and their pretreatment duration. The first, Group I, numbering 44 patients, represented patients with normal acid phosphatase, no hydronephrosis, and no bone metastases with a 59 per cent chance of 5 year survival following bilateral orchiectomy and stilbestrol therapy. The second, Group II, also numbering 44 patients, represented patients with metastases, having a 12 per cent chance of 5 year survival following identical anti-androgenic therapy.

It was shown that there appeared to be no significant difference in the pretreatment duration of symptoms in these two groups of patients. This suggests that these two groups represented cancers having widely varying biologic growth potentials.

The symptoms of dysuria, hematuria, and acute urinary retention occurred with approximately equal frequency in the two groups, but back pain and weight loss occurred far more frequently in Group II than Group I, and appear to be ominous symptoms strongly suggesting osseous or lymphatic dissemination of disease.

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CARCINOMA OF THE BREAST: A TEN YEAR APPRAISAL

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The purpose of this paper is to appraise the experience with cancer of the breast of one university hospital over a 10 year period. Studies of this sort, both large and small, have clearly documented what might be expected in a given series of patients with this lesion who were treated in an acceptable manner. Notwithstanding, each institution should have its own standard for comparative purposes and this study is presented to fulfill this basic need. Of subordinate value may be its use in adding to the sum total of experience with breast carcinoma.

The institution in which this study has been done had its beginning in 1941. In that year the generally accepted basic treatment for carcinoma of the breast was the so-called classical radical mastectomy of Halsted and Meyer, dating from 1894, and its adoption was quite natural. During the decade immediately following 1941 which was selected for this study, and continuing with increased vigor to the present time, there have been noteworthy departures from the general acceptance of radical mastectomy as the method of choice in the treatment of breast carcinoma. These departures have taken off at wide angles of divergence from the standard of radical mastectomy. In one direction, on the basis of a well known experience, McWhirter has suggested that equal if not better results might be expected with a less radical surgical approach to the management of carcinoma of the breast. Others have underwritten this suggestion. Contrariwise, others have revived and extended the operative attack on cancer of the breast to include areas of spread beyond the confines that previously had been determined as adequate in the classical radical mastectomy, reflecting the recent trend of more extensive surgery in many malignancies.

These opposing trends have created a healthy situation in our thinking in cancer of the breast. It has stimulated basic restudy of modes of spread and lymphatic drainage of the mammary gland. Refinements in the factors concerned in selection of patients have accrued. Variance in the many subtleties involved in prognosis have come to be appreciated. The factor of "*predeterminism*" transcending features of histologic type, grading, local and regional spread is being evaluated in mammary cancer as well as other malignancies. Hormonal dependence and its influence on tumor growth is being studied intensively.

In the midst of this era of healthy re-evaluation in mammary carcinoma, this study is presented. The majority of the patients whose cases are herein reported have been treated by radical mastectomy. A smaller number have been managed

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by simple mastectomy and irradiation. Neither procedure is advocated over the other. An analysis of the results with each is simply tabulated.

General Features: This modest experience comprises a total number of 247 histologically proved cases of carcinoma of the breast seen at the North Carolina Baptist Hospital from Jan. 1, 1941, through Dec. 31, 1950. Of this number, 240 patients have been followed until death or at least 5 years, giving a percentage follow-up of 97 per cent. Of the 7 patients not completely followed and, therefore, considered dead, 4 were Stage I, 2 were Stage II, and I was Stage III mammary cancer. There were 246 females and 1 male in this series.

One hundred and eighty-four radical mastectomies were done in this group of patients. Forty-eight patients underwent simple mastectomy, or a minor modification of a simple mastectomy. Ten patients were treated by irradiation alone and, of this number, 2 lived 5 years. Five patients had no treatment, either because it was not advised or it was declined by the patient. Of these 5 patients, 1 lived 5 years. There were 2 postoperative deaths in the group of patients who were operated upon, both deaths occurring in patients who had simple mastectomies. Each died of pulmonary embolism, 1 on the seventh postoperative day and the other on the tenth postoperative day. The operative mortality rate, therefore, in 232 patients operated upon is 0.8 per cent.

Gross Results in 247 Cases of Carcinoma of the Breast: In table 1, the gross results in the 247 cases of mammary carcinoma are tabulated according to the extent of the disease. An accepted classification of the stages of carcinoma of the breast is utilized. Tumors involving the breast only are classified as Stage I. Cutaneous change and ipsilateral palpable axillary nodes with breast tumor are considered Stage II. Ipsilateral supraclavicular nodes contralateral axillary nodes or fixation of the breast to the pectoral fascia denotes Stage III. Stage IV includes those patients who had mammary cancer with skeletal or visceral metastasis. For purposes of comparison, Stage I and II are considered "*theoretically curable*" carcinoma of the breast. Seventy-four and four-tenths per cent of 94 patients who had Stage I breast carcinoma survived for 5 years. Forty-five and two-tenths per cent of 115 patients who had Stage II survived for 5 years and the 5 year survival for 209 "*theoretically curable*" patients was 58.3 per cent. The 5 year survival for all patients is 52.6 per cent.

TABLE 1

Summary of results, breast carcinoma

Stage	Number	Alive 5 Years	Dead 5 Years	Not Followed, Assumed Dead	Per Cent 5 Year Survival	Died After 5 Years	Per Cent Gross Survival
I	94	70	20	4	74.4	10	63.8
II	115	52	61	2	45.2	14	33.0
I and II	209	122	81	6	58.3	24	46.8
III	29	8	20	1	27.5	3	17.2
IV	9	0	9	0	0	0	0
Totals	247	130	110	7	52.6	27	41.0

TABLE 2

Summary of results, radical mastectomy

Stage	Number	Alive 5 Years	Dead 5 Years	Per Cent 5 Year Survival
I	73	54	19	73.9
II	97	42	55	43.2
I and II	170	96	74	56.4
III	13	4	9	30.7
IV	1	0	1	0
Totals	184	100	84	54.3

TABLE 3

Radical mastectomy irradiated and not irradiated

Stage	Irradiated				Not Irradiated			
	Total	Alive 5 years	Dead 5 years	Per cent	Total	Alive 5 years	Dead 5 years	Per cent
I	33	26	7	78.7	40	28	12	70.0
II	63	25	38	39.6	34	17	17	50.0
I and II	96	51	45	53.1	74	45	29	60.8
III	5	1	4	20.0	8	3	5	37.5
IV	1	0	1	0	0	0	0	0
Totals	102	52	50	50.9	82	48	34	58.5

Carcinoma of the Breast Treated by Radical Mastectomy: One hundred and eighty-four of the 247 patients who had mammary carcinoma were treated by radical mastectomy. Table 2 summarizes the results following radical mastectomy. In Stage I carcinoma, radical mastectomy yielded a 5 year survival of 73.9 per cent, and in Stage II lesions, 43.2 per cent. Fifty-six and four-tenths per cent of the aggregate 170 patients, (Stage I and II) survived 5 years. The over-all 5 year survival rate of mammary cancer treated by radical mastectomy is 54.3 per cent.

It is of interest to note that in Stage I and II the 5 year survival is less than that given in the gross results of all cases of carcinoma of the breast. This, as will be seen subsequently, is a result of the better survival statistics in the 48 patients treated by simple mastectomy and irradiation.

The majority of patients undergoing radical mastectomy were irradiated postoperatively. From the data in table 3, it can be seen that a uniform policy regarding postoperative irradiation has not been followed. A substantial number of the first three stages of mammary carcinoma treated by radical mastectomy were not irradiated, which allows an interesting comparison. The survival statistics would indicate that irradiation increases the salvage of Stage I carcinoma, a situation in which one might expect little need for ancillary aid by definition of Stage I, in that the tumor is limited to the breast alone. In contrast to this, one would expect an increased salvage of patients in the more advanced stages although these figures tend to indicate the reverse. It is generally accepted that

TABLE 4

Radical and simple mastectomy

Stage	Scirrhous and Medullary				Intraductal and Comedo				Mucoid				Paget's			
	Total	Alive	Dead	Per Cent	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent
I	71	52	19	73.0	17	13	4	76.4	4	3	1	75	1	1	0	100
II	102	45	57	44.1	12	7	5	58.3	0	0	0	0				
I and II	173	97	76	56.0	29	20	9	68.8	4	0	1	0				
III	20	6	14	30.0	1	0	1	0	1	0	1	0				
IV	3	0	3	0	0	0	0	0	0	0	0	0				
Totals	196	103	93	52.5	30	20	10	66.6	5	3	2	60	1	1	0	100

TABLE 5

Radical mastectomy

Stage	Scirrhous and Medullary				Intraductal and Comedo				Mucoid				Paget's			
	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent
I	61	45	16	73.7	8	6	2	75.0	3	2	1	66.6	1	1	0	100
II	87	37	50	42.5	10	5	5	50.0	0	0	0	0	0	0	0	0
I and II	148	82	65	55.4	18	11	7	58.8	3	2	1	66.6	1	1	0	100
III	12	4	8	33.3	1	0	1	0	0	0	0	0	0	0	0	0
IV	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	161	86	75	53.4	19	11	8	57.8	3	2	1	66.6	1	1	0	100

postoperative irradiation does increase the 5 year survival of carcinoma of the breast. In this particular series it would seem that postoperative irradiation did not influence significantly the survival in patients treated by radical mastectomy.

Table 4 indicates the breakdown into pathologic type of the 232 surgically treated carcinomas of the breast. The division into the four groups; scirrhous and medullary, intraductal and comedo, mucoid and Paget's disease, is done so as a matter of convenience. A better and more simple division might be the inclusion of poorly differentiated and invasive scirrhous, medullary and mucoid carcinomas in one group; and the more differentiated, less invasive intraductal, comedo and Paget's type in another group. Inasmuch as previous reports on breast carcinoma from this institution have utilized the former division, it will be adhered to in this report.

Table 4 indicates the more favorable survival statistics in the intraductal, comedo and Paget's carcinoma of the breast as compared with the scirrhous, medullary and mucoid. This same situation obtains with respect to these various types treated by radical mastectomy, as is seen in table 5.

Carcinoma of the Breast Treated by Simple Mastectomy: Despite the general policy of radical mastectomy for mammary carcinoma in this institution, a minority of patients have been treated by simple mastectomy with irradiation. The following reasons were given in the clinical records for performing simple mastectomy: (1) the patient refused radical mastectomy. (2) the simple mastectomy was done for palliative reasons, and (3) the surgeon thought that simple

TABLE 6

Summary of results, simple mastectomy

Stage	Number	Alive 5 Years	Dead 5 Years	Per Cent 5 Year Survival
I	20	15	5	75.0
II	17	10	7	63.5
I and II	37	25	12	67.5
III	9	2	7	22.2
IV	2	0	2	0
Totals	48	27	21	55.3

TABLE 7

Simple mastectomy according to type lesion

Stage	Scirrhous and Medullary				Intraductal and Comedo				Mucoid			
	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent	Total	Alive	Dead	Per cent
I	10	7	3	70.0	9	7	2	77.7	1	1	0	100
II	15	8	7	53.3	2	2	0	100.0	0	0	0	0
I and II	25	15	10	60.0	11	9	2	81.8	1	1	0	100
III	8	2	6	25.0	0	0	0	0	1	0	1	0
IV	2	0	2	0	0	0	0	0	0	0	0	0
Totals	35	17	18	48.5	11	9	2	81.8	2	1	1	50

mastectomy was sufficient to take care of the patient's disease. This latter reason was seen particularly in patients with comedo and intraductal carcinomas and more frequently during the latter part of the decade of study. Experience with mammary carcinoma treated by simple mastectomy from 1941 through 1945 in this institution has been reported by Deaton and Bradshaw. This present report simply extends that study of simple mastectomies in this institution from 1945 through 1950.

During the 10 year period of study, 48 simple mastectomies for histologically proved mammary cancer were done. Table 6 summarizes the results from simple mastectomy according to the stage of the lesion. The five year survival of 20 Stage I lesions treated by simple mastectomy is 75 per cent as compared with 73.9 per cent 5 year survival of Stage I lesions treated by radical mastectomy. In Stage II lesions, the 5 year survival percentage is 63.5 per cent as compared with 43.2 per cent for radical mastectomy. Thus the 5 year survival rate for theoretically curable carcinoma of the breast treated by simple mastectomy is 67.5 as compared with 56.4 per cent 5 year survival in this same group treated by radical mastectomy. The greatest variation, of course, as seen in these figures lies within the Stage II carcinoma.

In table 7, mammary carcinoma treated by simple mastectomy tabulated according to the pathologic type of lesion is presented. It is seen that survival statistics in all types exceed comparable types treated by radical mastectomy.

COMMENT

The gross results in this series of carcinoma of the breast would suggest a more favorable 5 year survival in those patients treated by simple mastectomy and irradiation as compared to those treated by radical mastectomy. A correction for patients dying in the immediate postoperative period would tend to make the results following simple mastectomy even more favorable inasmuch as the only two deaths in this series were following simple mastectomy, which is 4 per cent of the total of patients so treated.

Nevertheless, there are other factors which must be taken under consideration which would tend to make the differences in results from these two modalities of treatment more apparent than real. The group of patients treated by simple mastectomy is relatively small compared to that treated by radical mastectomy.

Two additional factors may overly influence the results herein reported. In the first place, one might argue that since several of the patients treated by simple mastectomy were treated for palliative reasons alone, the more favorable lesions were reserved for treatment by radical mastectomy. One factor which would tend to disprove this is apparent from the study of the pathologic type treated by each type of mastectomy. It will be noted that the 11 patients with intraductal and comedo carcinoma treated by simple mastectomy represents 22.9 per cent of the total lesions treated by simple mastectomy. Contrasted to this, 9.7 per cent of the total lesions treated by radical mastectomy were intraductal and comedo carcinoma.

Table 8 summarizes the age of patients by decade when treated by radical and simple mastectomy. The average age of patients treated by radical mastectomy is 50.8 as compared with an average age of those treated by simple mastectomy of 55.2. Perhaps a more significant difference in the ages of these two groups might be indicated by the fact that only 3 per cent of patients treated by radical mastectomy were above 70 years of age; whereas 31 per cent of those treated by sinple mastectomy were above 70.

TABLE 8

Age of patients when treated

Decade	Radical Mastectomy			Simple Mastectomy		
	Alive	Dead	Total	Alive	Dead	Total
21–30	3	4	7	0	0	0
31–40	28	16	44	6	2	8
41–50	26	24	50	6	0	6
51–60	28	21	49	3	6	9
61–70	13	15	28	5	5	10
71–80	2	4	6	6	8	14
81–90	0	0	0	1	0	1
Totals	100	84	184	27	21	48

Average age radical mastectomy, 50.8. Average age simple mastectomy, 55.2. Percentage patients above 70: radical, 3%; simple, 31%.

SUMMARY

An experience with 247 consecutive cases of histologically proved cancer of the breast is presented. Survival statistics in 184 patients treated by radical mastectomy have been analyzed with regard to the stage of the lesion, pathologic type and age of the patient when treated.

The same features in a smaller group of patients treated by simple mastectomy have been tabulated. Although the gross survival of those patients treated by simple mastectomy exceeds that in the radical mastectomy group, the difference may be more apparent than real when considered in each instance from the point of view of pathologic type and age of the patient at the time of treatment.

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SURGERY OF THE ADRENAL GLANDS

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The adrenal glands consisting of a medullary portion derived from neurogenic ectodermal tissue and a cortical portion derived from primitive celomic epithelium are in reality two unrelated organs, each having an independent endocrine function. The medulla, being similar in derivation and histologic structure to the sympathetic ganglia, is the main source of epinephrine and nor-epinephrine formation in the body and a study of its physiology deals largely with the pharmacology of these two drugs. The cortex by comparison is infinitely more complex in its function, exerting far reaching and diverse effects on body metabolism, sex and growth patterns and body electrolytes. Surgical lesions of the adrenals are outlined in fig 1. As the physiology and biochemistry of these complex organs has become better understood, the surgical management of disease processes in which they are involved has been possible with increased safety and improved results. Nevertheless the field is still of such complexity that teamwork between the internist and surgeon is essential not only in the proper selection of patients for operation but also in preoperative and postoperative care.

MEDULLA

The adrenal medulla is derived embryologically from neurogenic ectodermal tissue and tumors of this organ are similar to those of other portions of the sympathetic nervous system. One group, sometimes listed as the neuroblastomas, has no endocrine function. These tumors most commonly occur in infancy and childhood and are variously classified, depending upon the maturity of the cell type, as sympathogonioma, sympathoblastoma or ganglioneuroma. In general these tumors tend to be malignant in children and benign in adults although the opposite may hold in any individual case.

Endocrine producing tumors of the adrenal medulla, the pheochromocytomas, are chromaffin cell tumors which produce both epinephrine and nor-epinephrine and cause symptoms similar to those produced by injection of epinephrine (fig. 2). These tumors usually are benign in nature and about 10 per cent occur outside the adrenal in which case they may be called paragangliomas. They usually are of small size although massive tumors as described by Colcock and Hull[1] may occur. In rare instances such as the case described by Davis and associates[5] pheochrome tumors may have functioning metastases.

Episodes of paroxysmal hypertension are the classical findings in cases of pheochromocytoma. Along with hypertension these patients usually have symp-

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CLASSIFICATION OF SURGICAL LESIONS
OF THE ADRENAL GLANDS

MEDULLA (Tumors)
- Immature Cell Type
  - *Sympathicogonioma*
  - *Neuroblastoma*
  - — *Non Endocrine*
- Mature Cell Type
  - *Ganglioneuroma*
  - *Pheochromocytoma* — *Endocrine*

CORTEX
- Hyperplasia
  - *Diffuse*
  - *Nodular*
- Tumors
  - *Adenoma*
  - *Carcinoma*

HETEROLOGOUS TUMORS

CYSTS
- *Lymphatic*
- *Hemorrhagic*

toms of palpitation, sweating, precordial distress, headaches and may show blanched cold extremities. As the disease progresses sustained hypertension may develop (in approximately one-third of the recorded cases)[18] making it difficult to differentiate this lesion from essential hypertension. Richards and Hatch[19] have described five different groups of patients with pheochrome tumors as follows: (1) paroxysmal hypertension; (2) sustained hypertension; (3) atypical hyperthyroidism; (4) hypertension, mild hyperthyroidism and mild diabetes; and (5) asymptomatic individuals who develop sudden collapse following minor trauma or surgery. Those cases which do not fall into the classical picture may prove exceedingly difficult diagnostic problems.

When pheochromocytoma is suspected from the clinical findings several diagnostic aids may be utilized to establish the diagnosis, although exploratory surgery may be necessary. Physical presence of tumor may be determined or presumed by information gained from urography or presacral insufflation of oxygen, and when combined these two procedures are excellent diagnostic tools. Aortography may be of value in selected cases. Adrenolytic drugs such as regitine®, dibenamine or benzodioxane which block the transmission of sympathetic nerve impulses at the myoneuric junction usually will produce a lowering of blood pressure in patients with pheochrome tumors and not in those with essential hypertension although there are cases in which blood pressure is not lowered. Other drugs such as mecholyl®, histamine and etamon® may be used to stimulate the release of pressor compounds in a patient with pheochromocytoma although they must be used with great caution. The adrenalytic drugs are of most value in those cases having sustained hypertension while the latter group is of value in those with paroxysmal hypertension. Neither group of drugs is an infallible diagnostic aid and negative results do not rule out the presence of

FIG. 2. Pheochromocytoma (below) and right adrenal gland(above) removed from a 45 year old man who had a 10 year history of sustained hypertension. The tumor was disk shape, weighing 63 Gm.

a tumor. Recently methods for studying the urinary catechol amines have been developed and it appears that in the future, these tests may be of great value in establishing the diagnosis of pheochrome tumors.

When the diagnosis is established or strongly suspected, surgical exploration is indicated. In planning the surgical approach it must be remembered that about 10 per cent of these tumors are located outside the adrenals, usually along the retroperitoneal sympathetic chain and that they may be bilateral. For these reasons a transabdominal approach is generally considered preferable since a general exploration of both glands and the retroperitoneal area can be carried out. Episodes of hypertension may occur during manipulation of the tumor and a precipitous fall may occur following its removal. Use of a short acting epinephrine competitor such as regitine® may be used to prevent the former while epinephrine or nor-epinephrine may be used as a supportive measure if indicated.

CORTEX

During recent years much laboratory and clinical research has been done in an effort to unravel the enormously complex snarl of adrenal cortical physiology, and much progress has been made. However, concepts are changing with such rapidity that statements made in a manuscript may well be superseded by the time the article appears in print.

For the most part surgery of the adrenal cortex is concerned with hyperfunction either on the basis of diffuse hyperplasia or as a result of tumor formation, although certain cortical tumors produce little or no physiologic changes.

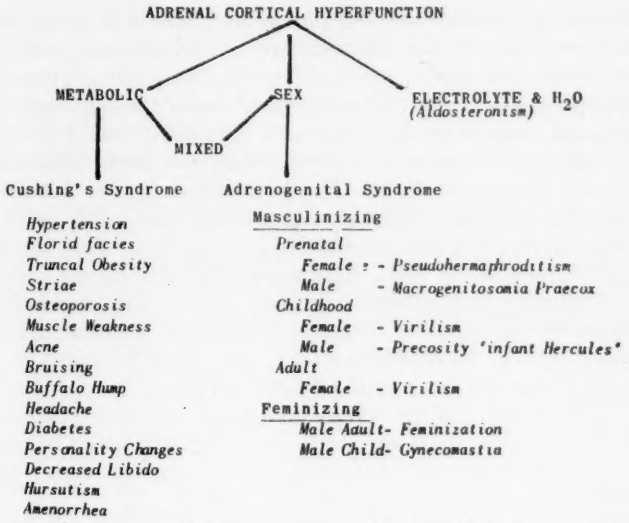

FIG. 3. Diagram showing the three major categories into which cases of adrenal cortical hyperfunction due to either tumor or hyperplasia, can be grouped.

Recently the therapeutic possibilities of total adrenalectomy have been studied in the management of certain specific widespread cancer of other organs, notably the breast and prostate.

Broadly speaking, the signs and symptoms produced by adrenal cortical hyperfunction can be divided into three general categories (1) those associated with metabolic alterations (Cushing's syndrome), (2) those with sexual changes (adrenogenital syndrome), and (3) those associated with electrolyte and water disturbances (aldosteronism), although it must be emphasized that considerable overlapping of these groups exists in many cases. It also is important to remember that the age and sex of the individual is an important factor in the changes produced by hyperfunction of the adrenal cortex. A classification based on the physiologic changes produced is outlined in figure 3.

Laboratory Features

Some 30 complex steroids have been isolated from the adrenal cortex and their chemical structures have been determined. The functions of certain of these substances such as cortisone are well understood while little is known about others. In general these hormones can be divided into three major categories: (1) the gluconeogenic, (2) the androgenic, and (3) the sodium-retaining.

The cortisone or gluconeogenic phase of adrenal activity is concerned chiefly with carbohydrate and protein metabolism and probably to a lesser degree the metabolism of fat. Of the various compounds studied thus far, the most important and potent hormones in this group are 11-hydroxy-17-dehydrocorticosterone (cortisone or compound E of Kendall) and 17-hydroxycorticosterone

(hydrocortisone). The important and far reaching effects of these substances both directly and indirectly through an interaction with other endocrine glands is becoming better understood, but their clinical usage in all types of disease states is not completely clarified. The manifestations of Cushing's syndrome are due largely to an excess of cortisone activity. The determination of the amount of urinary excretion of 11-oxysteroids is an indicator of corticoid activity. Both androgenic and estrogenic compounds are produced by the adrenal cortex. Since the tendency toward virilism usually predominates in adrenal tumors or hyperplasia, this phase of adrenal activity is sometimes called the androgen effect and cases manifesting these changes are referred to as the adrenogenital syndrome. Androgenic and estrogenic activity were formerly measured by bioassay methods which are far from satisfactory although chemical measurements are now available. One would expect a direct correlation between the degree of masculinization and the amount of urinary androgen, and between the intensity of feminization and the excretion of urinary estrogen, but this is not always the case in instances of adrenal tumors or hyperplasia. The ratio of one to the other as well as the amount utilized by the body have been suggested as more important than the actual total urinary excretion.

Of the many measurements of adrenal activity, the one most commonly in use probably is the determination of the urinary 17-ketosteroids. This test measures the non-phenolic, neutral, 17-ketosteroids comprising in general most of the substances having androgenic activity although certain androgens such as testosterone are not included and other substances having no androgenic activity are included. Since these substances measured by 17-ketosteroid determinations are elaborated both by the adrenal and by the male gonads, levels in the male are somewhat higher than in the female. Likewise the levels show a progressive increase with age, showing highest levels around age 40 following which a gradual decrease occurs. There are several different methods for determining the 17-ketosteroids each showing slight differences in normal values with a fairly wide normal variation. The normal adult excretion in mg. per 24 hours is around 15 for males and 10 for females. The neutral 17-ketosteroids can be further separated into alpha and beta fraction by precipitation methods. The alpha fraction representing 85 to 90 per cent of the total probably is derived from both the adrenal and the male gonad while the beta fraction representing the remaining 10 to 15 per cent most likely consists of excretion products derived only from the adrenal cortex. In adrenal tumors there is an increase in the percentage of the beta fraction. It can, therefore, be seen that determination of the neutral 17-ketosteroids while not a true index of adrenal androgenic activity is sufficient for the purpose of most clinical work especially if the alpha and beta fraction are obtained. It must be remembered also that the liver plays a major role in the conversion of the adrenosteroids into 17-ketosteroids and such levels may be altered significantly in liver disease.

Light has been thrown on the third, or electrolyte, phase of cortisone activity by the recent isolation and synthesis of aldosterone.[21, 25] This substance has 20 to 30 times the potency of desoxycorticosterone or DOCA and exerts an

effect on the renal tubules, the sweat glands, the salivary glands, the gastrointestinal tract and the shift between the intra and extra cellular compartments to cause retention of sodium, chloride and water and to increase the urinary excretion of potassium and phosphorus. The exact role of this substance in various disease states is as yet not clear but Conn[2] and others have described cases of chronic potassium depletion and alkalosis and suggested the name primary aldosteronism.

Cushing's Syndrome

In 1932 Cushing described the classical findings of truncal obesity, moonface, acne, hirsutism, striae, muscular weakness, depression of libido, amenorrhea, hypertension, polycythemia and diabetes in a patient having a basophile adenoma of the pituitary. This set of findings can be artificially induced by the prolonged administration of cortisone or ACTH.

While the controversy still smoulders over the question of whether these cases result from primary adrenal pathology (either tumor or hyperplasia) or primary pituitary disease (Kepler[14] found a basophilic adenoma in 50 per cent of cases) the clinical manifestations are those of adrenal cortical hyperfunction and therapy should be directed in that direction. Approximately 30 per cent of patients with Cushing's syndrome will be found to have an adrenal tumor, either adenoma or carcinoma, while the remaining 70 per cent have hyperplasia.[20] In those cases without tumor the disease is similar to Graves' disease of the thyroid and it has been shown that hyperfunction of the adrenal cortex can exist without gross enlargement of the glands (10 per cent).[3] The metabolic manifestations of Cushing's syndrome probably result from a hypersecretion of the 11-oxysteroids with a resultant increase in urinary excretion of this hormone. However, if adrenal androgenic or estrogenic production also is excessive, features of adrenogenitalism may coexist and it may be that excessive production of aldosterone is the cause of the water and electrolyte changes sometimes observed. Most cases of hyperplasia have a normal or slightly elevated urinary 17-ketosteroid level while in cases of tumor the level will most often be elevated. Many cases of Cushing's syndrome have an abnormality of calcium metabolism with resultant demineralization of bones, especially the vertebrae, demonstrable on roentgenogram. These cases usually show a marked increase in urinary calcium excretion. When adrenal cortical hyperfunction is due to tumor the problem is one of complete removal of the tumor. If hyperplasia is present or even if no gross enlargement can be demonstrated the present accepted treatment consists of complete removal of one gland and removal of a large portion of the remaining gland.

Adrenogenital Syndrome

In adrenal cortical hyperfunction due either to tumor or hyperplasia there may be a predominance of those hormones having an effect on secondary sex characteristics with little or no corticoid effects as seen in Cushing's syndrome. In most instances the androgenic hormones predominate with resultant masculinizing tendencies while in rare instances the estrogenic hormones predomi-

nate to produce feminization. Patients manifesting secondary sex changes due to adrenal cortical dysfunction are grouped together under the adrenogenital syndrome. This also has been referred to as adrenal virilism and interrenalism. The clinical findings in these cases will obviously vary greatly, depending upon the age and the sex of the individual affected as well as the predominate sex hormone produced. Statistically the pathologic basis of the adrenogenital syndrome is more apt to be tumor than hyperplasia.

When adrenal hyperplasia occurs prior to intrauterine differentiation of the fetal sex organs the resulting abnormality will be pseudohermaphroditism in the female or macrogenitosomia precox in the male with abnormalities of the genitourinary apparatus as indicated by the names.

In the female child adrenal cortical hyperfunction produces a picture of virilization, characterized by enlargement of the clitoris, appearance of pubic hair, deepening of the voice and rapid increase in size and weight. According to Wilkins[27] most, if not all, of these cases are due to tumor when the changes occur before the age of 10 or 12 years while they may be due to either tumor or hyperplasia after that age.

In the male child hyperadrenocorticism results in the so-called infant Hercules characterized by enlargement of the penis, appearance of pubic hair, deepening of the voice and an increase in size and muscular strength. Despite these changes the testes remain normal in size. Rarely the feminizing hormones may predominate with resultant pronounced gynecomastia. In either instance the underlying cause is most likely adrenal tumor although early virilization may result from adrenal hyperplasia or from an interstitial cell tumor of the testes.

In the adult female masculinization without the metabolic changes associated with Cushing's syndrome may be due to either adrenal tumor or hyperplasia. The masculinizing features include increased muscular development with a change of body contour, deepening of the voice, loss of libido, scanty menses, masculine pubic hair pattern and enlargement of the clitoris. Similar changes, of course, may be found in patients with arrhenoblastoma of the ovary. Clear cut cases offer little diagnostic difficulty; however, cases of mild hirsutism associated with obesity and menstrual changes (the so-called pseudoadrenal disorders) may be extremely difficult to differentiate.

Hyperadrenocorticism in the adult male usually results in Cushing's syndrome or at least the metabolic alterations are predominant. In rare instances, however, there is a predominance of estrogenic effects with resultant feminization. A review of the reported cases, numbering 28 in all, including an instance of a feminizing cortical carcinoma in a 26 year old Negro has recently been made.[9] This case was characterized by gynecomastia (fig. 4), impotence, a decrease in size of the penis and testicles and right upper quadrant pain. The level of urinary excretion of the 17-ketosteroids reached 600 mg. per 24 hours with a beta fraction of 60 per cent. There also was a huge increase in pregnanediol excretion, the 24 hour urinary level being 621.6 mg.

As stated previously the adrenogenital syndrome is usually, if not always, due

FIG. 4. True gynecomastia in a 26 year old Negro man having a feminizing carcinoma of the right adrenal.

to tumor when it occurs in individuals under the age of 10 or 12, while in the adult the underlying process may be either tumor or hyperplasia. If the patient has had symptoms and physical changes for many years, hyperplasia is the more likely cause although adenomas may be present for years without producing marked changes. Since the choice of treatment depends on whether or not a tumor is present it is important if possible to make this determination by methods other than surgical exploration. As discussed under another heading roentgenologic diagnostic aids may be helpful in demonstrating the presence of a tumor. Also laboratory determination may be of value. The urinary 17-ketosteroid level usually is elevated and when tumor is present the beta fraction frequently constitutes more than the normal 10 to 15 per cent of the total figure. It has been shown that the administration of cortisone to patients with cortical hyperplasia will produce a sharp fall in the urinary 17-ketosteroid excretion while no alteration results in hyperadrenocorticism due to tumor.[8] This test is of great help in differentiating tumor from hyperplasia but may not hold true in every instance.[16]

During recent years Wilkins[26] and others have shown that most cases of the adrenogenital syndrome due to hyperplasia can be managed by the administration of cortisone. This is based on the fact that the cortisone surpresses the elaboration of ACTH by the pituitary with consequent diminution of adrenal function including the hypersecretion of androgens. Several patients, particularly in the younger age groups, have been managed for several years in this fashion with favorable results. When tumor can be demonstrated or is strongly suspected, surgical exploration is indicated.

Aldosteronism

Until recently the water and electrolyte phase of cortical activity was known clinically chiefly in Addison's disease, characterized by a deficiency of the hormones controlling water and electrolyte metabolism. Desoxycorticosterone acetate or DOCA has been used with moderate effectiveness to control the water and electrolyte imbalance present in cases of adrenal cortical insufficiency. It also had been observed that the amorphous fraction remaining after all known crystalline substance had been removed from adrenal extracts was effective in maintaining life in adrenalectomized animals and the name electrocortin was given to the unidentified hormone. During the past three years this substance having 20 to 30 times the effectiveness of DOCA has been isolated, crystallized and its properties characterized. The name aldosterone has largely replaced the older term, electrocortin. The relationship of aldosterone to certain diseases is being studied and Conn has reported a patient having intermittent tetany, parathesia, muscle weakness, a low serum potassium and high serum sodium who was found to have an adrenal cortical adenoma which was removed with subsequent disappearance of symptoms. Other similar cases have been described and this condition of primary aldosteronism will undoubtedly be observed with increasing frequency.

DIAGNOSTIC AIDS

The history and physical findings of the various adrenal abnormalities have been outlined as the syndromes were discussed. These findings may be so clear cut as to leave little doubt about the diagnosis on clinical grounds alone; however, there often is considerable overlap between the classical Cushing syndrome and the adrenogenital syndrome. Likewise tumors of the testes or ovary may produce endocrine changes similar to those of hyperadrenalism. In addition the so-called pseudoadrenal disorders in which mild hirsutism, obesity and menstrual changes are present may be extremely difficult to differentiate from a true adrenal abnormality. It is with this borderline group of cases that the various biochemical studies are of most value. The adrenopressor and adrenolytic drugs used in the diagnosis of pheochrome tumor have already been discussed. Likewise the significance of the various steroid determinations have been outlined in the section on laboratory studies.

When the diagnosis of adrenal disease is made or strongly suspected, whether it be of the cortex or the medulla, it is important to know if possible whether there is a tumor present and if so, which adrenal is involved. Urinary pyelography either intravenous or retrograde, presacral oxygen insufflation and aortography used singly or in combination may demonstrate the presence of an adrenal tumor.

The procedure of injecting air into the perirenal areas has been replaced by presacral injection of oxygen. This latter procedure has been used in large numbers of cases without difficulty. In most instances 500 to 700 cubic centimeters of oxygen introduced through a spinal needle inserted beneath the tip coccyx and into the presacral space will outline the kidneys and adrenals. The

FIG. 5. Combined retrograde pyelogram and presacral oxygen insufflation showing downward displacement of the right calyceal pattern by a huge tumor of the right adrenal gland.

oxygen will flow upward when the patient is in the upright position, and one side or the other can be better visualized by placing the patient with that side uppermost.

When a large adrenal tumor is present the kidney usually will be pushed downward and the calyceal pattern, as outlined by intravenous or retrograde pyelography, will be distorted. Combined use of presacral oxygen insufflation and pyelography may be of value (fig. 5).

The adrenals and their blood supply may be visualized by translumbar injection of an opaque medium into the aorta. This procedure can be carried out with relative safety; however, it does require anesthesia and in most instances probably should be reserved for special cases.

THERAPEUTIC ADRENALECTOMY

In recent years there has been considerable interest in the possible effects of bilateral adrenalectomy on certain disease processes having dependence upon adrenal hormones. In 1945 Huggins and Scott[12] reported 4 cases of bilateral adrenalectomy done on patients with disseminated prostatic cancer and since that time several series of cases by these and other authors have been reported. While the early results were encouraging insofar as palliation was concerned it is apparent that most cases can be managed with the usual hormonal measures with equal results. Following this work the possible role of total adrenalectomy in the management of advanced carcinoma of the breast was explored. Huggins

and Dao,[11] who have had the most extensive experience with this therapy, have recently reviewed 100 cases with noteworthy regression of cancer and alleviation of pain in 40 per cent of cases. On the basis of their studies certain criteria have been established to insure best results and the reader is referred to these authors for details. Other series of cases have shown similar results and it would appear that bilateral adrenalectomy has a definite place in the management of certain cases of breast cancer. Likewise a few cases of carcinoma of the breast in males have been treated by combined orchiectomy and bilateral adrenalectomy with encouraging remission.[4]

The association of hypotension with Addison's disease and of hypertension with Cushing's syndrome and pheochromocytoma has led to the investigation of bilateral adrenalectomy in the management of cases of essential hypertension. Jeffers, and associates,[13] have combined subtotal adrenalectomy (95 per cent) with sympathectomy while Thorn, and associates,[24] have used bilateral total adrenalectomy without sympathectomy. Both series of cases have been studied carefully and it would appear that the procedure should still be regarded as experimental and its widespread clinical adoption be reserved pending further investigation.

SURGICAL CONSIDERATIONS

Once it has been decided that surgical intervention is indicated several factors peculiar to adrenal physiology must be considered in the preoperative and postoperative management of patients undergoing adrenal surgery, and the operative approach must be planned to best accomplish the desired results in the individual patient. The adrenals may be approached transabdominally, transthoracicly, or retroperitoneally. No single approach is suitable for all types of pathology which may be encountered and even with the best exposure removal of adrenal tumors may be difficult. Bilateral adrenalectomy without adequate replacement therapy is incompatible with life, the essential factor being the cortex, the loss of medullary function being of little significance.

Pheochromocytoma: In the surgical management of pheochrome tumors two important considerations apply: (1) these tumors may be bilateral and in some instances the tumor may be outside the adrenals along the sympathetic chain and (2) manipulation of the tumor during operation may precipitate dangerous hypertensive crises and following removal of the tumor the blood pressure may fall precipitously to shock levels (fig. 6). Because of the occasional bilaterality or extra-adrenal location of these tumors the transabdominal approach is preferable since it affords a better exposure of both glands and the paraaortic region. A transverse upper abdominal incision with transection of both recti has been found most satisfactory, although a vertical incision or bilateral subcostal incisions have been used by some. The retroperitoneal approach may be used, although exploration of the paraaortic area is somewhat limited. In order to minimize possible harmful effects of paroxysmal hypertension brought on by manipulation of the tumor during operation, Grimson, and associates,[7] have suggested the use of epinephrine competition before and during operation. Because of its

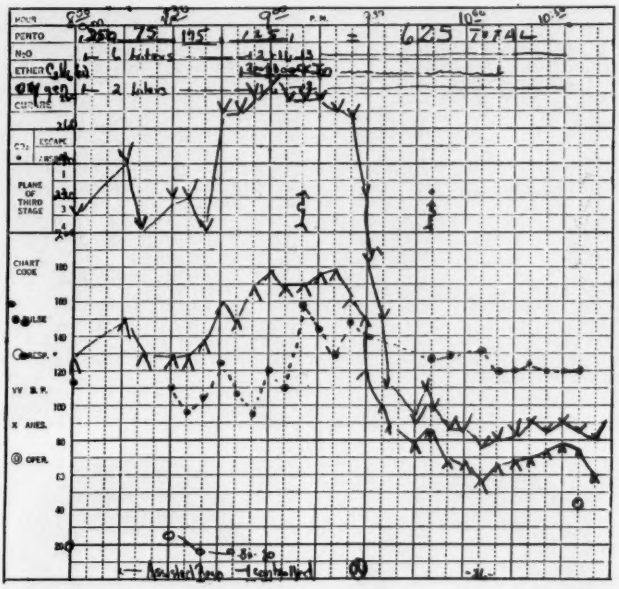

FIG. 6. Anesthesia chart of a patient during removal of a pheochromocytoma. Note the increase in blood pressure during manipulation of the tumor and the precipitous drop in pressure following removal.

shorter action regitine® in 5 mg. doses is preferred; however caution must be used to avoid difficulty in handling the drop in pressure which follows removal of the tumor. This drop usually can be managed without difficulty by adding nor-epinephrine to the intravenous solution being administered at the time of operation. Should the anticipated drop in pressure fail to occur following the removal of a tumor, the presence of a second tumor should be suspected and a careful search of the area again be made. In rare instances when portions of both adrenals must be removed or are traumatized cortical insufficiency may occur requiring cortical replacement therapy.

Cushing's Syndrome: Once the diagnosis of Cushing's syndrome has been made surgical therapy probably is indicated (fig. 7). Suppression of the anterior pituitary by irradiation or by the use of testosterone has not been generally effective although pituitary irradiation and unilateral adrenalectomy have been used with fair success[22]. When a tumor is present, removal of the tumor along with the involved gland in most instances is indicated. Since function of the opposite adrenal usually is suppressed by the hyperfunctioning tumor, special measures must be taken to avoid serious if not fatal adrenal insufficiency in the postoperative period. The measures usually employed consist of stimulation of the suppressed gland by the administration of ACTH during the preoperative preparation, supplemental sodium before and after operation and cortisone substitution as needed. Huggins[10] has outlined in detail the procedure to follow in

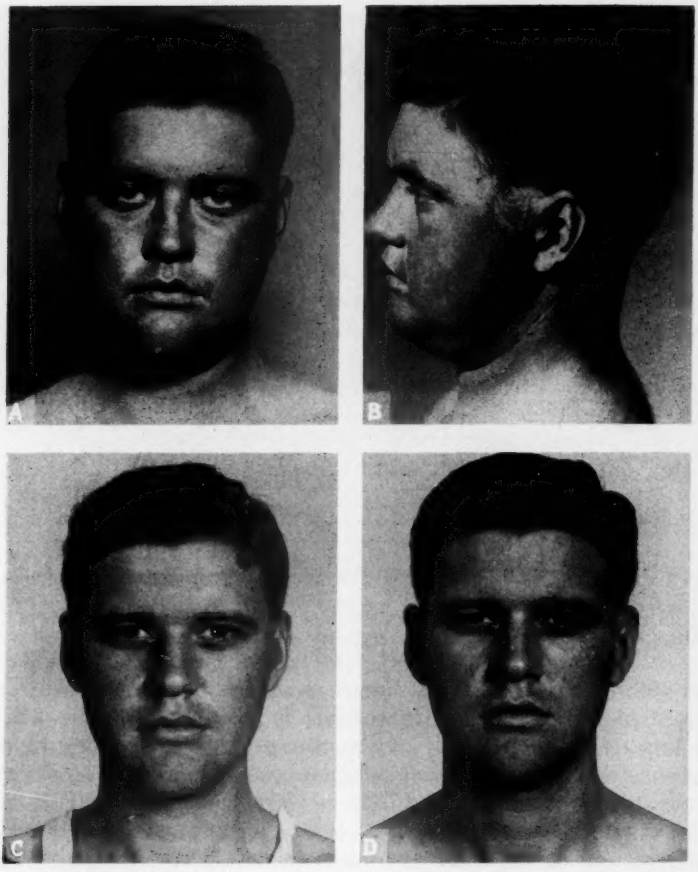

FIG. 7. A 27 year old man with typical Cushing's syndrome. A and B preoperative. (Note evidence of previous pituitary irradiation.) C. Five months following subtotal adrenalectomy. D. Ten months following operation.

managing the patient who is having bilateral adrenalectomy. In recent years both cortisone and hydrocortisone are available in intravenous forms and several authors[6, 18] have followed a simplified schedule with considerable success. No special preoperative preparation is carried out until the day of operation when 100 mg. of hydrocortisone in 5 per cent dextrose and saline is given prior to the induction of anesthesia. Further hydrocortisone then is given intravenously to control blood pressure as needed (usually about 250 mg. total). Intramuscular cortisone then can be substituted and then oral cortisone when the patient's general condition permits. Desoxycorticosterone usually is not necessary except following complete adrenalectomy and then not until several days after operation is its use necessary. In the presence of tumor the degree of suppression of

FIG. 8. Photograph to show bilateral posterior subdiaphragmatic incisions for simultaneous exposure of both adrenals. The twelfth rib is removed on each side.

the contralateral gland may vary considerably and no hard and fast rules can be made. The remaining gland may be stimulated by the administration of ACTH if needed and an increased intake of sodium chloride may be indicated.

Except for instances in which a tumor can be localized definitely preoperatively, exposure of both adrenals is indicated. Unlike medullary tumors those of the cortex are not found in an extra-adrenal location except for rare instances.[17] We have found that bilateral simultaneous exposure of both adrenals can best be carried out through bilateral subdiaphragmatic retroperitoneal incisions with the patient prone (fig. 8). This approach is similar to that described by Hugh Young except that oblique incisions are made over the twelfth rib and the rib removed. The lumbodorsal fascia is opened and the retroperitoneal space entered below the diaphragm without entering the pleura, although no harm is done should the pleura be inadvertently opened if it be recognized and closed. This approach permits easy visualization of the glands. If necessary the incision can be carried cephalad and the eleventh or tenth ribs transected to afford wider exposure. The transthoracic or extended lumbar incision may afford better exposure of large tumors.

The histologic determination of malignancy or benignancy in adrenal tumors may not always be simple. However, in those patients in whom benign neoplasm have been removed, the results have been uniformly good, while few of the patients with frank malignancy survived.

As previously stated Cushing's syndrome associated with bilateral adrenal hyperplasia is in many ways analogous to Graves' disease of the thyroid. Adrenal hyperplasia may be associated with multiple nodules similar to nodular goiter and there may be hyperplasia without gross enlargement of the glands. It is not surprising, therefore, that surgical therapy has been directed along lines

similar to those used in the treatment of hyperthyroidism. The experience of Albright and associates[15] as well as Sprague[23] and others have shown that subtotal adrenalectomy has produced good results in a large proportion of cases. Sufficient gland must be removed to insure continuous remission and sufficient tissue should remain to avoid adrenal insufficiency. This is best accomplished by removing one gland in its entirety and approximately 80 to 90 per cent of the remaining gland. The two groups previously mentioned also have outlined the approach one should follow in the surgical management of Cushing's syndrome and in general this provides an excellent guide. Preoperative preparation of the patient is carried out as outlined above. Operative plans should be made for exposure of both glands. We prefer the subdiaphragmatic posterior approach as previously described. If the first adrenal gland explored is atrophic, the contralateral gland probably is involved in tumor which should be removed. Replacement therapy is, of course, essential. If the first adrenal gland explored is large the opposite gland will also be enlarged and subtotal adrenalectomy (90 per cent) is the indicated treatment. If the first adrenal gland explored is normal in size, this gland and its opposite are probably hyperplastic and subtotal adrenalectomy is indicated.

The following case report illustrates an unusual manifestation of hypercorticism:

CASE REPORT

C. H., a 39 year old white man, was admitted to the Psychiatric Service of the Kansas City Veterans Hospital on Sept. 3, 1955 because of mental depression and suicidal tendencies. It was believed by the Neuropsychiatric Service that this patient would benefit from electric shock therapy. Routine films of the thoracic and lumbar spine showed marked osteoporosis and consultation was obtained relative to this. Upon further questioning it was found that the patient had noticed an increasing weakness and easy fatiguability during several months prior to admission. There also had been a diminution of libido and decrease in sex activity. Physical examination was not remarkable. None of the stigmata of Cushing's syndrome such as truncal or facial obesity, purplish striae, ecchymosis or acne were present. The blood pressure was 120/80.

Laboratory studies were carried out in an effort to determine the underlying cause of this patient's osteoporosis. The serum calcium phosphorus and alkaline phosphatase levels were found to be normal. The glucose tolerance test was found to show a diabetic type curve. Repeated examination of the urine showed an increase in calcium excretion. The total circulating eosinophil count was markedly depressed to 2 per cubic mm. The urinary 17-ketosteroid excretion was found to be 19 mm. per 24 hours. The urinary 11-oxysteroid excretion levels were markedly elevated, being 11 mg., 16.2 mg., and 18.4 mg. per 24 hours on three different occasions in two different laboratories. These levels were some of the highest ever observed in either laboratory. Intravenous urography done simultaneously with retroperitoneal oxygen studies failed to demonstrate an adrenal tumor.

Despite the absence of physical signs of Cushing's syndrome and normal blood pressure, a diagnosis of hyperadrenocorticism was made and surgical exploration recommended. After routine preoperative preparation the adrenals were explored simultaneously using bilateral posterior subdiaphragmatic incisions with removal of the twelfth rib on each side on Dec. 7, 1955. Both adrenals appeared to be normal in size and location and no tumor could be found. There was noted some nodularity of the left gland. Subtotal adrenalectomy was carried out by removing the entire left adrenal gland and approximately 80 per cent of the right gland. The left adrenal weighed 5.6 Gm., the removed portion of the right adrenal

weighed 3.1 Gm. Pathologic study of the removed specimen showed hyperplasia without hypertrophy of the cortex of both adrenals with cortical nodules.

The postoperative course has been entirely uneventful. The patient's general feeling of well being has returned to normal although he continues to complain of slight weakness. In the opinion of the psychiatrist mental symptoms and attitude improved dramatically following operation. Postoperatively the 11-oxysteroid levels have returned to normal, the total circulating eosinophils have returned to normal and the urinary calcium excretion is normal.

Although insufficient time has elapsed since operation to be certain of the eventual course, it is our opinion that this patient represents a case of hyperadrenal corticalism due to adrenal hyperplasia without hypertrophy and without some of the more obvious changes generally associated with Cushing's syndrome.

Adrenogenital Syndrome: As previously outlined differentiation between tumor and hyperplasia as the underlying cause of masculinization or feminization usually can be made with a fair degree of certainty and those patients in whom the changes are secondary to adrenal hyperplasia can in most instances be managed by administration of cortisone. In doubtful cases cortisone can be administered as a test to determine whether the urinary 17-ketosteroid level declines to normal levels. In children below the age of 10 years or in adults, tumor should be strongly suspected.

As opposed to the situation in tumor producing Cushing's syndrome, adrenal tumors causing adrenogenital syndrome do not produce suppression of the opposite adrenal. For this reason elaborate preoperative preparation to avoid serious postoperative adrenal insufficiency is not necessary in these cases. No single operative approach can be used for all patients. In those instances when the tumor can be localized preoperatively, the choice of approach is simplified. In our experience the transthoracic or combined thoracoabdominal incision provides optimal exposure for large tumors. In the female it must be remembered that ovarian arrhenoblastoma may produce a picture indistinguishable from adrenal cortical tumors and the surgical approach should be planned so that the ovaries can be examined.

SUMMARY

The adrenal glands consisting of medulla and cortex, each having a separate embryologic origin, present a complex challange in diagnosis and treatment. As the biochemistry and physiology have become better understood the surgical management of disease processes in which these complex organs are involved has been possible with increasing safety and improved results.

The medulla usually becomes of concern to the surgeon when involved by tumor either of the non-endocrine, neurogenic type more commonly seen in childhood or by the functioning pheochromocytomas. Although paroxysmal hypertension is the most common manifestation of these tumors, sustained hypertension is present in approximately 30 per cent of cases. In addition to the pharmacologic aids to diagnosis such as the regitine and histamine tests, determinations of the urinary catechol amine levels show promise as a helpful tool in diagnosing these difficult problems.

Surgery of the cortex is concerned chiefly with hyperfunction either due to diffuse hyperplasia or to tumor formation. The manifestations may be (1) those associated with metabolic alterations (Cushing's syndrome), (2) those with sexual changes (adrenogenital syndrome) and (3) those associated with electrolyte and water disturbances (aldosteronism) although considerable overlapping of the three groups exists in many cases. Determination of the urinary excretion levels of the 17-ketosteroids and 11-oxysteroids may be of diagnostic help, and urinary pyelography combined with presacral oxygen injection is of great value in localizing or determining the presence of an adrenal tumor. When hyperadrenocorticism is caused by tumor, surgical removal is indicated. Cases of adrenogenitalism, when caused by adrenal hyperplasia, can be managed medically by the administration of cortisone. Cushing's syndrome, resulting from adrenal hyperplasia, is best managed by subtotal adrenalectomy.

The case history is presented of a patient exhibiting serious mental disturbances as well as vertebral demineralization and laboratory evidence of increased adrenal cortical activity but without the physical stigmas of Cushing's syndrome and without hypertension, who showed marked improvement following subtotal removal of hyperplastic adrenal glands. It is believed that similar cases will be diagnosed and treated with increasing frequency as adrenal physiology is better understood.

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THE MANAGEMENT OF THE BRONCHIECTATIC PATIENT WHO CANNOT BE CONSIDERED A CANDIDATE FOR SURGERY

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In March of 1955 I recorded in the American Surgeon 705 cases of patients who had bronchiectasis and who had been submitted to surgery in the past 10 years in three Baltimore hospitals, and the experience gained from that method of treatment in the management of bronchiectasis.[1] In reviewing those cases there were two groups of patients which were not included in that article, patients who were not considered candidates for surgery. This paper deals with those two groups of patients in order to complete the picture of bronchiectasis as we have seen it in our clinical experience.

Of these two classes, Group I encompassed those patients with minimal involvement of the bronchi. Group II included the far advanced bronchiectatic patients with emphysema.

Minimal bronchiectasis is defined here as involvement of less than the four basilar bronchi of the lower lobes, or half or less than half of the middle lobe or lingula, or one segment or less of the upper lobe. If tuberculosis is the instigating factor this definition does not aptly apply as the approach to therapy is different.

In Group I there were 47 cases of minimal disease which fell in the usual two types of (1) sacular and (2) cylindrical forms. The etiology of the sacular type seem to be purely acquired rather than congenital when minimal, and purely inflammatory, whereas the cylindrical type seemed to have a basic allergic or asthmatic etiology in each instance.

No patient was submitted to surgical removal of the diseased lung whose symptoms did not include hemorrhage or who had not had multiple bouts of pneumonitis with broncho or lobar pneumonia. Although surgical consultation was asked for in this minimal group, it seemed to be the opinion of various surgeons and various internists that medical therapy, not surgery, was indicated. The volume of sputum could not be considered an indication for surgery. Nine of the 47 patients could be followed through successive admissions for bronchopneumonia or febrile pulmonary illnesses in whom bronchographic studies showed progression of the disease with extending involvement, making them eventual candidates for surgery. The remainder of this group, i.e., those that could be followed by office records, have not extended their disease to any serious degree and on various medical routines, have not extended the disease to where pulmonary resection would be indicated by the symptoms which they exhibit. The

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medical routine which seems the most satisfactory and rapid in the recovery of the patients consists of (1) placing the patient at bed rest for 5 to 8 days, (2) giving a broad spectrum antibiotic based on predominant organism sensitivity, in the usual dosage, (3) giving hydrocortisone or its derivatives in large dosage, i.e., 500 mg. the first 24 hours, 300 mg. the second and third days and a maintenance dose of 100 mg. thereafter for upward to 3 weeks depending on the development of toxic signs such as ankle edema, (4) the use of bronchial dilators and (5) expectorant cough mixtures. Occasionally bronchoscopic suction was used as an adjunct in the patient with large amounts of sputum. Twice daily exercises of postural drainage were routinely performed under supervision.

In the group of cylindrical bronchiectasis, even those with demonstrable bronchial stenosis by bronchograms, the disease seemed to be entirely reversible when certain restrictions were added to the above medical regime. The restriction of smoking cigarettes, and a number of these patients presented an allergic picture of sensitivity to cigarettes and the use of tobacco in any form, was mandatory for any improvement. Patients also were encouraged to seek dust free occupations and particularly avoid some of the solvent and cleaning fluid fumes.

Several of these patients have been through the outlined drug therapy two or more times after the recurrence of symptoms with more easily obtained responses on the second and third course of therapy. None of these patients have extended their disease to the point of seeking surgical intervention.

Two patients in the minimal group have developed a typical middle lobe syndrome or Brock's, the presented symptom in one being moderately severe hemoptosis, in the second persistant severe chest pain radiating to the epigastrium, right shoulder blade and back. The second patient had had blood streaked sputum but was not sufficiently alarmed to seek aid until the development of severe pain.

Group II. The emphysematous patient is included in this paper because many of them seem to be the end result of long standing pulmonary abuse from bronchiectasis. In the history of a large number the volume of sputum had decreased over the years as the dyspnea increased with barreling of the chest. Bronchographic studies frequently revealed cylindrical bronchiectasis with stenosis at various points in large or smaller bronchi. In reviewing 50 of the cases of patients in whom bronchograms were performed only 2 were submitted to thorocotomy and these for reasons other than excision of bronchiectatic segments. In the first patient thorocotomy was performed to suture a bronchopleural fistula which had become permanent and created 3 successive pneumothoracies. The second was operated upon because of the development of an infected, air-fluid level containing bleb. It has been our experience that when a bleb appears in such fashion, that the instigating disease is a lung carcinoma. These patients also are the poorest risk from the standpoint of anesthesia, developing anoxia in the hands of even the most skillful anesthetist.

The previously outlined medical routine is of substantial benefit to the majority of these patients. Benefits can be judged by the increase in the ability to physical work or exertion such as walking. We recently have added pneumoperitoneum

with significant improvement in the patient with emphysema in carrying on respiration without the use of accessory muscles and increasing his ability to perform work with less fatigue. The amount of air in the peritoneum must be maintained weekly at about 600 to 800 cc. There seems to be no way to predict which patient will benefit from pneumoperitoneum without trial. Not all patients are helped.

In the opinion of a large group of practicing physicians, patients with minimal bronchiectasis as defined herein or patients with emphysema of a bronchiectatic background are not candidates for major pulmonary excisional surgery. The medical means outlined effect complete regression of the disease, and in certain instances, either cure, or effect considerable improvement.

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THE INDETERMINANT PULMONARY CAVITY

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The writer has undertaken this presentation with substantial reservation since admittedly the patients to be considered under such a title suffer from a variety of diseases, the clinical manifestations of which range from a near lack of symptoms to the presence of truly alarming signs such as major hemoptysis. In addition fortunately they constitute only a small segment of thoracic surgical experience. Last, they are only artificially identifiable as a group in whom objective diagnostic procedures have yielded negative results.

However on encountering the patient with a solitary indeterminant pulmonary cavity, worn by weeks or months of study and distressed by indecision and conflicting advices, one cannot but wonder at the professional attitudes which finally lead to such situations. Undoubtedly in the not distant past almost all of them would have been clinically diagnosed as having tuberculosis, with its then-staggering implications. Thus assuming an obligation to demonstrate tubercule bacilli before making a firm diagnosis of tuberculosis represents a major advance in professional thought. One hesitates even to suggest compromise with such objectivity yet one cannot escape recognition that we have discovered so many different ways in which to be objective. Indeed at times we seem addicted to routines which incorporate every known approach to a given situation.

In respect to the problem here being considered we can examine the sputum directly and with a variety of handling and staining methods. Cultures may be prepared to meet the conditions favored by a broad spectrum of organisms and one can attempt demonstration of the disease by inoculation of experimental animals. Unfortunately one must wait many weeks for the results of these latter studies but of course in the meantime the patient can be bronchoscoped and the bronchial tree irrigated, the material so obtained then being available for repetition of all of the foregoing tests. And of course the aspirated gastric content need not escape study. One may observe the skin's reaction to a number of antigens which can be applied in varying concentrations. Similarly serologic reactions may be investigated. And one dare not overlook the possibility of both simple and complicated radiologic studies: special projections, laminography, bronchography, etc. And any of these tests may be repeated, indeed many usually are, not once but several times.

Now I do not wish to suggest that these are not valuable examinations. Obviously they are, each and every one of them. Indeed in some patient studies they may all need to be employed. All I ask is that we consider them in relation to the patient with the solitary, localized pulmonary cavity. Are we not now generally in accord that the solitary homogenous pulmonary opacity is best managed

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TABLE I

Final diagnosis in 20 patients with preoperatively indeterminant pulmonary cavities

Specific inflammations	7
Coccidioidomycosis	4
Histoplasmosis	1
Tuberculosis	1
Indeterminate	1
Cysts	11
Bronchiectatic	5
Bronchial	3
Inflammatory	2
Bullous emphysema	1
Miscellaneous	2
Oil granuloma	1
Chest wall lesion	1
Total	20

by what amounts to an excision biopsy? Further is it not also true that increasing numbers of patients with proved localized tuberculous pulmonary cavitation are being subjected to elective local or segmental resection? May one not ask what diseases productive of such lesions are best managed by other than excisional therapy? Or to state the question even more directly, had one of the 20 diagnoses listed in table I been firmly established during any part of the exhaustive clinical workup, would not the patient have been recommended for operative treatment?

For these were the final diagnoses encountered in 20 such situations at the Walter Reed Army Hospital during the past 2 years. In many instances the correct diagnosis, although not proved, was strongly suspected during the period of preoperative study. It also must be admitted that not infrequently the presumptive diagnosis was incorrect. Further one must hasten to add that in a small series such as this, several potential offenders are not represented, not the least important of these being the excavated primary lung carcinoma.

The unusual nature of patient selection in a military medical service complicates comparison with civilian practice although the basic fundamentals of the issue remain the same. Some idea of incidence may be gained from the observation that during this same 2 year period 79 patients with solitary pulmonary opacities were resected. The sex and age distribution of the patients whose cases are here reported was as follows: males—14, females—6, ranging in age from 17 to 44 years, average—30 years. The cavities were equally distributed between the two lungs and as between the upper and lower lobes. At operation two lesions were found to be extrapulmonary. One was a cystic oil granuloma of the pleura occurring years after a temporary oleothorax. The other was a nonspecific abscess of the pleura and inner aspect of the chest wall.

The following detailed case report is typical of the problem presented by these patients.

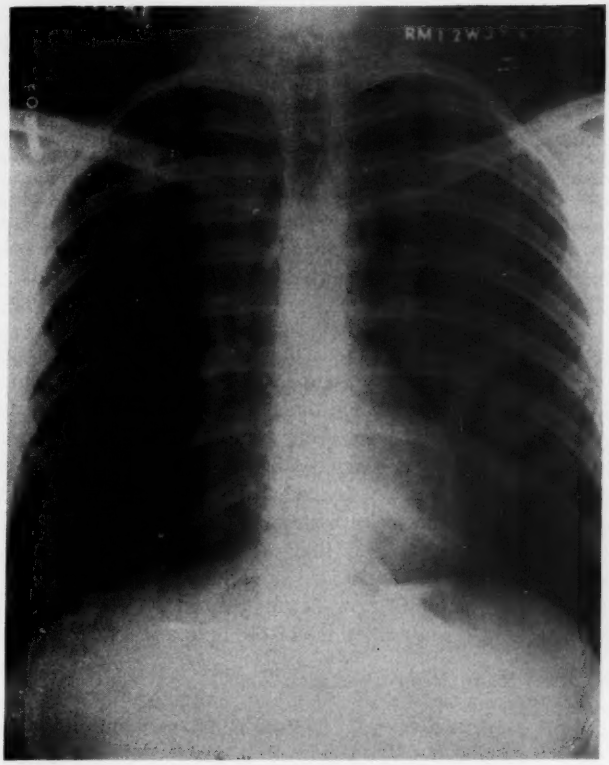

FIG. 1. Roentgenologic appearance of right apical cavity due to coccidioidomycosis

CASE REPORT

This 21 year old white man entered the Army in October 1953, had his basic training in Texas and was afterward stationed on the East coast. His past history was otherwise significant in that one year before hospitalization he had experienced a one week episode of blood-streaked sputum. He did not feel ill at that time and did not seek medical advice. The present illness began in July 1955, and was characterized by anorexia, weakness, easy fatiguability and moderate weight loss. He first requested medical assistance on Sept. 10. This resulted in a 13 day period of hospitalization during which time the right apical cavity seen in figure 1 was demonstrated. His skin reaction to tuberculin and coccidioidin was found to be negative and acid-fast bacilli could not be identified in several sputum specimens. Sputum cultures and animal inoculation studies were begun. A presumptive diagnosis of pulmonary tuberculosis was made. The patient was referred to the Walter Reed Army Hospital, being admitted there on Oct. 21. Physical and routine laboratory examinations were negative. He continued an afebrile course. No change could be detected in the pulmonary lesion. Direct examination was made of 12 sputum collections, 3 gastric samples and 1 bronchial washing, these materials also being used to start cultures from 4 sputum collections, 2 gastric samples and the 1 bronchial washing. Serologic findings included

negative reactions to the febrile agglutinins: typhoid, paratyphoid, proteus, brucella and tularemia; negative complement fixation titers for histoplasmosis, coccidioidomycosis and blastomycosis; and negative collodion agglutination test for histoplasmosis. Bronchoscopy was negative as were numerous cytologic studies of the sputum and bronchial washings. Repeated radiologic examinations were done including laminagrams and bronchograms. These clearly defined and localized the cavity. Finally on Dec. 7, 1955, still without a definitive diagnosis, the patient underwent apical segmental right upper lobectomy. He was well by Christmas. The pathologists were able to demonstrate the sporangia and endospores of Coccidioides immitis in stained sections of the surgical specimen and this organism was also cultured therefrom. During the month following the patient's discharge from the hospital the preoperative cultures and animal inoculation studies were reported as being negative.

SUMMARY

Thus in summary we have an instance of a patient undiagnosed after 3 months of intensive evaluation. With apical segmental resection of the lesion a definitive diagnosis was made possible and simultaneously the patient was treated in such fashion as to insure prompt recovery. But would not a similar definitive course have been followed had a firm diagnosis been established at any point curing the patient's preoperative testing. Indeed the only practicable effect of such a fortuitous development would have been the earlier institution of treatment.

It is the writer's intent to suggest that excision biopsy of such lesions not be reserved as merely the last of a long list of diagnostic procedures. Surely a studied reappraisal of this problem will make easier the lot of those unfortunate patients found to have a solitary cavity of the lung.

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EDITORIAL

TISSUE COMMITTEES

In recent years there has been a great improvement in professional standards of hospital care. This has been due to a variety of factors, not the least of which has been the activities of the Joint Committee on Accreditation. One of the relatively new developments in this hospital picture is the Tissue Committee, which has assumed a very powerful role. Few will deny that the work of these groups is of great value, and that much of the improvement in surgical care has been brought about by their activities. For the most part it would seem that members of these committees have worked long and faithfully and unselfishly. Nevertheless, it would appear that certain dangers and injustices may come about if the greatest care is not exercised by the members of this powerful group.

First let us analyze the membership of the Tissue Committee. This will vary greatly in different hospitals. However, a typical committee may consist of a pathologist, surgeon, anesthesiologist, gynecologist, dermatologist, etc. This group sits as a jury to scrutinize the work of the surgeons in the hospital. There is no doubt that the pathologist is peculiarly qualified in this duty. The surgeon also, by virtue of his training and experience, is able to render valuable opinions, provided that his judgment is not warped by personal opinions and feelings towards his fellow surgeons, many of whom may be his competitors. But what of the other members? What qualifications do they have to pass judgment on the work of the surgeon? For all practical purposes these men are amateurs who are passing on the skill and judgment of professionals, and may be poorly qualified to appreciate the difficulties the surgeon may have in deciding such problems as whether to operate or not, when to operate, what type of operation to perform, etc. It reminds me of a statement some years ago by a nationally known surgeon who made a remark something like this: "I would much rather operate before a group of experienced surgeons than before a group of students. The students constitute a much more critical audience because they have not themselves experienced the difficulties and problems that the experienced surgeons have and this makes the latter group much more tolerant and sympathetic to the problems encountered."

Let us suppose now that the shoe is on the other foot—that a miscellaneous group of staff members would pass judgment on the work of the pathologist, the anesthesiologist, the radiologist, the dermatologist, etc. I am sure these groups could well point out errors in diagnosis on the part of the pathologist and radiologist, and could point out instances of poor anesthetic administration, etc., and I am quite sure that these groups would feel that their critics do not have a very sound foundation for determining the quality of their work and might even object to such a jury passing judgment on them. But today it is the surgeon who is the target of all the criticism. It has become a popular indoor sport to point out and publicize the errors in diagnosis, the number of normal appendices removed, the number of normal uteri and ovaries that are removed, etc.

But what about the internist? Doesn't he make any errors in diagnosis and treatment? Who passes on the quality of his work? What about the dermatologist, neurologist, etc.? Or to carry the same line of reasoning into surgical specialties, how many normal tonsils are removed, and how many patients subjected to hemorrhoidectomy really need the operation?

This is not meant to be a condemnation of the Tissue Committees. On the contrary, I approve of them wholeheartedly and believe that for the most part they do a good job. They give freely of their time and energies and deserve a great deal of credit. Rather this is a warning and a suggestion that they use great care and that they do not carry their work to an extreme. It is a plea for them to be fair, impartial and reasonable. It should be pointed out that an over critical attitude toward the diagnosis of appendicitis, for example, may make a surgeon so fearful of removing a normal appendix that he may delay the operation too long with danger or even tragedy to the patient. Such instances have come to our attention. Unfortunately, there is no specific test which will make a diagnosis for us in all cases, and one is forced to rely heavily upon the judgment and the integrity of a surgeon. Mistakes are made by the greatest surgeons and diagnosticians. This does not mean in all cases that they have not used great care and judgment. It is only when the mistakes become too frequent that they should be called to account for them. It would be fine if the pathologists found acute appendicitis present in 100 per cent of the appendices which are removed with the preoperative diagnosis of appendicitis but, unfortunately, this is a utopia which is not attainable with our present knowledge and diagnostic facilities. There probably is an irreducible minimum below which we cannot go with reasonable safety. Although this has not been well defined it appears that it is somewhere in the neighborhood of 10 or 15 per cent. It would appear doubtful on the basis of our present knowledge that we should strive to get much below that.

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